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Contents

A multi-phase study on the impact of a psychiatry learning module on knowledge about common psychiatric disorders and their treatment for residents under training at the University of the East Ramon Magsaysay Memorial Medical Center

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Abstract

Introduction Physicians are often challenged when faced with patients with possible psychiatric problems. Their capacity to identify, diagnose, and manage psychiatric illnesses are often undermined by inadequate knowledge regarding psychiatry. The study aimed to develop a psychiatric learning module and evaluate its efficacy in increasing the knowledge of common psychiatric illnesses and their management among residents.

Methods In phase I, a review of records of patients admitted in the service hospital who were referred to Psychiatry was done. Participants for phases II to IV included residents from the departments which had the most number of referrals. In phases II and III, a focus group discussion and a survey, respectively, were done to identify residents' perceived needs regarding psychiatry. Based on phases I-III, a psychiatry learning module was developed. In Phase IV, a pre-and post-intervention study design was utilized, with the intervention being the administration of the learning module. Participants' knowledge regarding common psychiatric conditions was measured using a written examination at baseline, immediately after the module, and 3 months after the module.

Results There were 60 referrals to the Department of Psychiatry in 2011, mostly from Internal Medicine, Clinical Neurosciences, Ophthalmology-Otorhinolaryngology, and Obstetrics-Gynecology; the most common reason for referral was for evaluation and management of a primary psychiatric condition. Phases II and III identified the most common perceived reason for referral to be management of acute behavioral changes and the most common preferred topic for the learning module to be assessment and screening for psychiatric conditions. In phase IV, the participants' knowledge significantly increased from baseline both in the immediate and delayed post-module examination.

Conclusion The development and administration of a psychiatry learning module was found to be efficacious in significantly increasing the residents' knowledge regarding common psychiatric illnesses and their management.

Key words: psychiatric disorders

Recent developments in medicine have identified a global paradigm shift in health care systems from a highly targeted type of health care where patients are immediately brought to a specialist, to a system which has as its focal point the general practitioner and the family care physician.[1] In mental health, research in consultation-liaison psychiatry has highlighted the importance of shared care between psychiatrists and other physicians. Research has shown that a significant number of patients with psychiatric disorders are brought to their primary care physicians before referral to psychiatrists for care.[2] This leads to a potential treatment gap between the initial consult and definitive treatment that could span years and may lead to worse outcomes for the patient. In response to these needs, the WHO has published a document highlighting the importance of mental health care in the primary care setting which the United States, United Kingdom, Russia and Italy followed.[3, 4] South Africa has also provided for the integration of mental health care into state services.[5]

In the Philippines, mental health services lag behind general health care services. Health care professionals are not adequately trained in mental health diagnostics and management. Provision of mental health care services is also handicapped by the cultural stigma attached to mental illness, lack of trained psychiatrists, and inappropriate distribution of available mental health care resources.[6] As a consequence, Filipino patients with psychiatric illnesses have an increased tendency to present to primary care physicians or other medical specialists with symptoms which may be psychological in origin (i.e. fatigue, vague pains).

Worldwide, a higher proportion of patients visiting a general practitioner may not be aware that they are suffering from a mental health problem often expressed through somatic symptoms.[7] International reviews have noted that up to 30% of all family practice patients may have significant psychiatric morbidity.[3] Finally, more than half of all mentally ill patients are cared for by non-psychiatrists.[8]

These findings must also be viewed in the light of current epidemiological trends in mental health. Neuropsychiatric disorders account for six of the 10 leading causes of disability and represent 12.3% of disability adjusted life years lost; this is expected to reach 15% by 2020.[6] In 2002, the WHO estimated that 154 million people globally are suffering from depression, 91 million from alcohol use disorders, and 25 million from schizophrenia.[9] These alarming numbers are expected to continue rising in the future decades. Despite the awareness of these challenges, psychiatric syndromes remain one of the most complex and least-understood illnesses in the medical setting. Health professionals, including primary care physicians and physicians with specialties in other fields, are often challenged when faced with patients with psychiatric problems. Their capacity to identify, diagnose, and manage psychiatric illnesses are often undermined by several factors such as preconceived beliefs about psychiatry, inadequate knowledge, and lack of specific skills.[6]

In spite of this, mentally-ill patients have greater contact with primary care physicians than they do with psychiatrists.[3] Since physician competency in the psychosocial aspects of medicine is most strongly related to residency training, residents from various specialties are a good population to target when addressing knowledge discrepancies regarding psychiatric illnesses.[10] Increasing their knowledge about psychiatric syndromes will enhance their capacity to recognize psychiatric problems, respond effectively to these problems, and utilize appropriate avenues for referral when necessary. In providing basic learning modules to residents, it is hoped that this research will help reduce the gap between a patient's first medical consult and his receipt of appropriate psychiatric treatment. To date, no such psychiatry learning module for residents has been developed. Such a learning module would provide residents with increased awareness of mental health problems among medically ill patients, knowledge of diagnostic nosology with respect to psychiatric patients, and basic approaches in the treatment of the mentally ill. The aim of this research was to formulate and evaluate the efficacy of a psychiatry learning module in increasing the knowledge of common psychiatric illnesses among the residents in a private training hospital.

Methods

This was a four-phase study conducted in the Service Hospital of a private training medical center in Quezon City from December 2011 to October 2012. A chart review was conducted in the first phase to determine the nature of referrals to Psychiatry from other departments. Qualitative and quantitative needs assessments were conducted on residents from the referring departments in the second and third phases, respectively. In the last phase, the referring residents underwent a teaching module developed from the needs assessment. They were evaluated before and after the module.

Phase I: Review of Medical Records

The charts of patients admitted to the Service Hospital from January to December 2011 who were referred to the Department of Psychiatry were retrieved

and the following information was extracted: demographic data, psychiatric diagnosis, global assessment of functioning (GAF) on admission, GAF on discharge, change is GAF scores, duration of confinement, referring department, and reason for referral. The patients' diagnoses were coded using the Diagnostic and Statistical Manual, 4th Edition, Text Revision (DSM-IV-TR) criteria. The referring departments were Clinical Neurosciences, Internal Medicine, Obstetrics-Gynecology, Ophthalmology-Otorhinolaryngology, Pediatrics, and Surgery. Descriptive statistics were used to summarize and analyze the demographic data, psychiatric diagnoses, source of referral, and reason for referral utilizing the Statistical Product and Service Solutions (SPSS) version 16. Confidentiality and anonymity was maintained.

Phase II: Qualitative Needs Assessment

Residents from the top four referring departments identified in Phase I were recruited. Those who gave their consent participated in one of several focus group discussions (FGD) conducted by the investigator. The FGDs were guided by open-ended and closed-ended questions which centered on residents' attitudes regarding patients with mental illnesses, their level of comfort in handling these patients, common reasons for referral to the Psychiatry service, perceived difficulties in handling patients with psychiatric comorbidities, and their perceived need for a psychiatry learning module. The questions were reviewed by an expert consultation-liaison psychiatrist prior to administration to check for applicability of the items.

Manual content coding and framework analysis were utilized to analyze the data gathered. Thematic frameworks were identified by classifying and indexing data and answers that were consistent throughout the focus group discussions. Data reduction was done by comparison and contrast, and by combining similar quotes. The data were assessed according to the context of the responses, internal consistency, frequency, extensiveness, and response specificity. The results were then synthesized in a tabular and narrative form.

Phase III: Quantitative Needs Assessment

A survey tool was developed in consultation with a psychiatrist and pilot-tested. The residents who participated in Phase II were made to answer the survey regarding the need for a basic psychiatry learning module, reasons for patient referral to the service, and preferred topics for the learning module. Further suggestions for the learning module were also gathered. The data were summarized using descriptive statistics. The non-parametric Kruskal-Wallis test and post-hoc analyses were done to test for differences among the responses of the residents from the various referring departments.

Phase IV: Implementation of Learning Module

The residents who expressed the need for a basic psychiatry learning module and participated in the needs assessment phases were asked to undergo the learning module. Anonymity was maintained by coding the participants' identities. Assuming a 10 point mean difference in test scores from baseline, with 90% power to detect a significant difference, the calculated sample size was 35 participants at the 0.05 level of significance. A learning module was developed by the researcher based on the qualitative and quantitative needs assessment. The module was a PowerPoint presentation consisting of *core* and *specific knowledge* learning material. Core knowledge information included epidemiological trends in psychiatric illnesses, assessment and management of psychiatric emergencies or acute behavioral changes, an overview of common psychiatric conditions in the institution, including diagnostic criteria from the DSM-IV-TR, and basic therapeutic guidelines by the WHO. Common psychiatric conditions reviewed in the core knowledge information included major depressive disorders, bipolar disorders, schizophrenia, and substance use disorders. The specific knowledge component consisted of a variety of learning material tailored according to each department's specific needs. The content of the specific knowledge component per department are listed in Table 1.

Table 1. Contents of specific knowledge component lectures.

Department	Topics
Clinical Neurosciences	Breaking the Bad News Delirium
Internal Medicine	Delirium Overview of Psychopharmacological Agents Psychotropic Drug Interactions
Obstetrics and Gynecology	The Stages of Grief Sexual Abuse and Assault Postpartum Depression
Ophthalmology and Otorhinolaryngology	The Stages of Grief Breaking the Bad News

The primary outcome measure was a 25-item knowledge-based multiple choice examination consisting of 15 core knowledge and 10 specific knowledge questions. A post-course evaluation tool using a 5-point Likert-type scale was developed to measure the participants' level of satisfaction with the learning module. It assessed the participants' views on the efficacy of the module, content, speaker, relevance and overall rating. All tools were validated and pilot-tested under the guidance of a senior psychiatrist and a consultation-liaison psychiatrist.

The module was conducted by the investigator herself among the residents of the four referring departments. Hand-outs were given to all participants in order to facilitate their learning. The knowledge-based examination was given before, immediately after the session, and three months after the module to assess the participants' baseline knowledge, the efficacy of the intervention, and knowledge retention over time. The sessions, including the pre- and post-test, and evaluation lasted 1 ½ hours.

The post-module evaluation was administered to assess the residents' views regarding the efficacy of the course, including the content of the module, the speaker, the relevance of the module, and an overall rating of the module. It was designed as a five-point Likert-type scale, ranging from strongly disagree (1) to strongly agree (5). The content subcomponent assessed the module's ability to help the participant understand the prevalence and diversity of psychiatric problems, enhance knowledge regarding common psychiatric problems and specialized topics, and its appropriateness for the intended audience. Statements for the speaker subcomponent assessed the speaker's ability to present the module clearly and effectively, clarify content in response to questions, and knowledge regarding the topics covered. The last several statements from the relevance subcomponent assessed applicability to practice, appropriateness for specialty needs, and assistance in helping participants gain ideas for future practice. At the end of the evaluation, suggestions and comments for future learning modules were elicited. Finally, the participants were asked if they would recommend the module to other residents.

The results of the knowledge-based examinations were analyzed using paired-samples T-tests to assess for immediate learning and retention of information, while the post-course evaluations were summarized using descriptive statistics.

Results

Phase I: Review of Medical Records

Sixty inpatients were referred to the Psychiatry service from January 01 to December 31, 2011. The following diagnoses were noted after a review of their charts:

Axis I Psychiatric Diagnoses

Majority (70.0%) were diagnosed with a functional disorder, while the rest had a psychiatric disorder due to a general medical condition. Of those with a functional Axis I disorder, 17 (28.3%) were considered to have adjustment disorder. This was followed by major depressive disorder (n=11, 18.3%), schizophrenia (n=7, 11.7%), and substance use disorders (n=5, 8.3%).

Axis II Psychiatric Diagnoses

Of the 60 patients referred, only 7 (11.6%) met the criteria for a comorbid Axis II diagnoses: six were diagnosed with a personality disorder and the other was diagnosed to have mental retardation. The most common personality disorder diagnosed was borderline personality disorder (n=3, 5%).

Axis III Diagnoses

Cancer was the most common general medical condition of the patients referred to the Psychiatry Service, and together with ingestion of a toxic substance, post-partum, and benign ocular conditions requiring enucleation, comprised 56.6% of cases.

Axis IV Diagnoses

The psychosocial stressors of patients consisted of several large categories: coping with a general medical condition was the most frequent (50%), financial constraints (18.3%), poor primary support (10%), and unemployment (8.3%). Other stressors included marital conflict, recent death of loved ones, and sexual abuse.

Axis V Diagnoses

Fifty-eight percent of the patients had admitting and discharge global assessment of functioning (GAF) scores of 61 to 90 units. Three-fourths of the patients also had higher discharge GAFs, denoting an improvement in function upon discharge. One patient who expired in the

hospital was included in the analysis of admitting GAFs but excluded from that of the discharge GAF.

The medical service referred 25 of the patients, and together with ophthalmology and obstetric consults, accounted for 73.3% of the 60 referrals. A large number of the patients (28.3%) were referred to the Psychiatry service for evaluation and management of a possible primary psychiatric condition such as schizophrenia or major depression.

Phase II-III: Qualitative and Quantitative Needs Assessment

Focus group discussions were held with residents from each of the four departments with the highest number of referrals. Their characteristics are presented in Table 2. Key thematic frameworks which consistently appeared throughout the focus group discussions are presented in Table 3.

Table 2. Most common general medical conditions in patients referred to the Department of Psychiatry.

General Medical Condition	N	Percent
Cancer (i.e. signet ring adenocarcinoma, retinoblastoma, acute myelocytic leukemia)	11	18.3
Chemical/Corrosive Gastrointestinal Injuries 2 to Ingestion of Toxic Substances	9	15.0
s/p Normal Spontaneous Vaginal Delivery	8	13.3
Benign Ocular Pathology Necessitating Enucleation	6	10
Alcoholic Liver Diseases	4	6.7
Community-Acquired Pneumonia	3	5.0
HIV/AIDS-Related Diseases	3	5.0
Complicated Urinary Tract Infection	3	5.0
Other Illnesses	13	21.7
TOTAL	60	100

Table 3. Most common department sources of referrals to the Department of Psychiatry.

Source of Referrals	Frequency	Percent
Internal Medicine	25	41.7
Ophthalmology and Otorhinolaryngology	11	18.3
Obstetrics and Gynecology	8	13.3
Clinical Neurosciences	6	10.0
Surgery	5	8.3
Pediatrics	5	8.3
TOTAL	60	100.0

Qualitative Needs Assessment

Most of the residents found psychiatric patients to be difficult to handle, unpredictable, violent, and "scary". This resulted in a low level of comfort when handling patients with psychiatric illnesses; most felt that they were ill-equipped to provide good psychiatric care for the patient. In turn, the participants were also hesitant to formally diagnose and manage psychiatric problems in their patients – their most common reaction would be to immediately refer the patient to the Psychiatry service. Barriers to care resulting in these difficulties included communication problems, lack of exposure to psychiatric patients, lack of familiarity with psychiatric medications, and a lack of knowledge with regard to assessment and diagnosis of psychiatric syndromes. All the participants concurred with the need for a psychiatric learning module.

Quantitative Needs Assessment

The most common reason for referral to the Psychiatry service across all departments was acute behavioral changes and the most common preferred module topic was assessment and screening for psychiatric conditions. These are shown in Tables 4 and 5.

Table 4. Demographics and training characteristics of study participants (N = 35).

Age	28.4
Gender	
Male	10
Female	25
Year Level	
1	11
2	10
3	8
4	6
Department	
Clinical Neurosciences	5
Internal Medicine	11
Obstetrics and Gynecology	8
Ophthalmology / Otorhinolaryngology	11
Preferred Practice Type	
Public	5
Private	20
Mixed	10
Preferred Practice Setting	
Rural	9
Urban	26

The reasons for referral varied across departments and a post-hoc analysis using the Mann-Whitney U test showed the differences to be significant, as shown in Table 6. On the other hand, a comparison of preferred module topics revealed the residents' preference for the assessment and screening for psychiatric conditions and overview of common psychiatric conditions. This is shown in Table 7. Upon post-hoc analysis using the Mann-Whitney U test, significant differences were found between departments for breaking the bad news, psychopharmacological management of acute behavioral changes, and overview of psychopharmacological agents.

Table 5. Key thematic frameworks identified in the focus group discussions.

Key Thematic Frameworks	Supporting Statements from Data Gathered
Negative impression of psychiatric patients	"Hard to address aggression…" "Crazy, violent." "Antsy and hard to pacify."
Discomfort in handling psychiatric patients	"Takot ako. . . Refer to Psychiatry please." "We have a lack of experience." "Walang masyadong background. [Limited background]."
Difficulties encountered in handling psychiatric patients	"Always an element of surprise." "Difficulty in eliciting information." "Communication barriers. . ."
Needs in a psychiatry learning module	"Yes, how to tell patients the bad news…" "How to manage patients post-op…" "How to diagnose . . . with diagnostic labels." "What medications to give. . . "

Table 6. Most common reasons for referral: Survey responses from the Department of Internal Medicine.

	N	Minimum	Maximum	Mean Std.	Deviation
Acute Behavioral Changes	11	1.00	3.00	1.2727	.64667
Continuing Care	11	3.00	7.00	5.2727	1.55505
Family Therapy and Counselling	11	5.00	7.00	5.9091	.83121
Management of Suicidal Cases	11	1.00	2.00	1.9091	.30151
Psychotherapy/Clearance for Surgical Cases	11	4.00	7.00	5.8182	.98165
Psychotherapy for Coping with a Chronic Medical Illness	11	1.00	5.00	3.0909	.94388
Management of Oppositional/Difficult Patients	11	3.00	7.00	4.7273	1.19087
Valid N (listwise)	11				

Table 7. Most preferred topics for the learning module: Survey responses from the Department of Internal Medicine.

	N	Minimum	Maximum	Mean Std.	Deviation
Assessment and Screening for Psychiatric Conditions	11	1.00	7.00	2.8182	1.88776
Breaking the Bad News	11	3.00	7.00	5.1818	1.47093
Continuing Care for Psychiatric Patients	11	1.00	7.00	6.1818	1.77866
Psychopharmacological Management of Acute Behavioral Changes	11	1.00	5.00	2.1818	1.32802
Overview of Common Psychiatric Conditions	11	1.00	5.00	2.8182	1.25045
Overview of Psychopharmacological Agents	11	2.00	6.00	3.2727	1.34840
Psychotherapy for Oppositional / Difficult Patients	11	4.00	7.00	5.3636	.80904
Valid N (listwise)	11				

These results support the assumption that while all residents need a basic psychiatry learning module in order to provide them with an overview and assist them in the assessment of common psychiatric conditions, each department had unique reasons for referring patients. This was accompanied by individualized preferences for topics in the learning module. In this light, the addition of a specialized subcomponent for the learning module to address each department's specific needs would increase its relevance to their practice. Again, all participants responded positively when asked about the need for a psychiatry learning module.

Phase IV: Implementation of Learning Module

Of the original sample in phases II and III, 33 residents participated in the learning modules, examinations, and post-course evaluations (attrition 5.7%). The mean scores of the samples were considered as a whole, but subgroup analysis was performed.

Immediate and retentive learning

When the total sample population was considered, there was a significant improvement from baseline scores immediately after the module, with a mean difference of 6.39 points ($P < 0.01$, paired T-test). While there was a loss of information over time, the 3-month post-module mean score was still significantly higher from the baseline mean score with a mean change of 3.51 ($P < 0.01$, paired T-test). When the departments were considered individually, results showed a similar trend with the overall findings (Table 8), except for one department whose residents' 3-month post-module scores did not differ significantly from their baseline scores or immediate post-module examination scores.

Post-course evaluations

The mean quantitative rating was 43.6 (from a possible maximum score of 50) for all participants; the ophthalmology residents gave the highest rating (46.9). The mean qualitative overall rating was 4.7, which was between good to excellent. When suggestions for future modules were gathered, majority of the participants did not endorse any particular recommendation, while five participants suggested that the module be conducted over the period of several days to maximize learning. All 33 participants said that they would recommend the module to other residents in the future.

Discussion

Phase I of the study identified the type, prevalence, and sources of the psychiatric referrals. Phases II to IV of the study clearly demonstrated a perceived need for a psychiatry learning module for the residents. It is likely that the module served to meet a previously unvoiced need for the enhancement of knowledge regarding psychiatry, and the focus group discussions served as a forum in which this need was brought to the fore. The focus group discussions (phase II) and surveys (phase III) showed that the residents were aware that psychiatric needs were present in their patients, a finding which was supported by phase I of the research (review of referrals). Participants from all the departments endorsed their need for a learning module that included an overview of

Table 8. Most common reasons for referral: Survey responses from Clinical Neurosciences.

	N	Minimum	Maximum	Mean Std.	Deviation
Acute Behavioral Changes	5	1.00	2.00	1.2000	.44721
Continuing Care	5	1.00	2.00	1.8000	.44721
Family Therapy and Counselling	5	3.00	7.00	4.0000	1.73205
Management of Suicidal Cases	5	4.00	7.00	5.6000	1.14018
Psychotherapy/Clearance for Surgical Cases	5	3.00	7.00	5.6000	1.67332
Psychotherapy for Coping with a Chronic Medical Illness	5	4.00	7.00	5.2000	1.30384
Management of Oppositional/Difficult Patients	5	3.00	6.00	4.6000	1.14018

common psychiatric conditions and assessment and screening for psychiatric conditions. Phases II and III served to identify other topics of interest within the field of psychiatry which the participants felt would be relevant to the practice of their specialty. These showed significant differences in the topics that the residents preferred to be included in the specialized module and were considered in the development of the learning module. Finally, there was general agreement among the participants that a psychiatry learning module would be a valuable step towards addressing their needs toward the enhancement of their knowledge regarding psychiatric illnesses in general.

Phase IV included the administration of the learning module, examinations, and post-module evaluation. The modules were developed to target the perceived needs for each department, with core specialized knowledge components. The examination scores showed significant increases in the knowledge of the residents from baseline. The immediate post-course results showed the most significant improvements of scores compared to baseline. While a significant loss of knowledge was detected over a period of three months, the participants' knowledge as measured by the delayed post-module evaluation was still significantly higher than their baseline scores, with the exception of one department. The failure to detect significant long-term improvements in this department's scores, however, may have been due to the small sample size (n = 5) compared to other departments, leading to a decrease in statistical power. Post-module evaluations generally revealed favorable results, with all participants rating the module as good to excellent. Quantitative overall ratings were likewise high, with the participants unanimously recommending the module for future use.

At the time this research was conducted, there was no other local study that sought to qualitatively and quantitatively assess and respond to residents' needs regarding psychiatric illnesses through educational measures. The strengths of the study lie in the methodical assessment and verification of these needs, as well as the development and administration of psychiatric learning modules in an effort to respond to these needs. The modules contained core and specialized knowledge components, which was done to maximize the response to each department's individual need. This is the first local study which assessed the outcome of such a learning module, and the original data and outcomes which demonstrated the efficacy of a psychiatry learning module are strengths of the research. It is hoped that, as partial fulfillment of the goals of consultation-liaison psychiatry, this will contribute to the enhancement of medical professionals' knowledge regarding psychiatric illnesses.

Another strength of the study is its ease of administration. In a developing country such as the Philippines, low-cost educational modules, such as that which was developed in the research, serve as a valuable tool in the dissemination of knowledge among medical professionals. As highlighted in the review of literature, Filipinos have a high prevalence of mental illnesses which are largely unmet due to a severe lack of access to basic mental health care. In addition to this, such a module would assist in imparting psychiatric care to our countrymen through integrating mental health care into the provision of other public health services nationwide, as envisioned by the Department of Health's latest National Objectives for Mental Health.[11, 12]

The limitations of the study are: 1) The study was done in a private institution which had a limited number of residents compared to other hospitals. This led to a relatively small absolute sample size which may have diminished the statistical power of the sample. 2) The efficacy of the module may have been enhanced if it been administered over a longer period of time. In fact, this was the only suggestion for improvement noted in the post-course evaluation. However, since the modules were not mandatory to the residents, the time constraints of the residents did not allow for a module longer than 1 1/2 hours. 3) Although the study reflected improvement in the residents' knowledge of common psychiatric illnesses and their management, this may not reflect a concomitant improvement in their clinical practice. A longitudinal study would have to be conducted in order to determine the consistency in their knowledge improvement over an extended period of time.

The following are therefore recommended: First, it is suggested that future administration of the module be done during a scheduled time to ensure the residents' concentration, as well as provide time for the expansion of the module to include simulated patient scenarios. Second, given the decrease in the residents' delayed (3-month) post-test scores, the administration of such modules may be helpful if conducted in a more regular basis (i.e., annually) to improve knowledge retention. Finally, a larger replication study is recommended in order to validate the findings of this study.

In summary, the study was able to fulfill its stated objectives and, in particular, highlighted the perceived need for a psychiatric learning module for residents from other departments. It sought to respond to this need through the development of a psychiatry learning module, which was effective in significantly increasing the participants' knowledge regarding common psychiatric illnesses and their management. Upon post-module evaluation, the participants endorsed the utility of the

module and unanimously recommended the module for future use with other residents.

The researcher is optimistic that this study has helped to address current concerns of residents, and proposed a feasible approach to increase knowledge regarding psychiatry among them as part of an endeavor to address the present mental health needs of our countrymen.

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Patient empathy among medical students

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Abstract

Introduction Medicine at its core is a human service profession with the goal of caring for patients. It is expected that a physician practices medicine that combines the life sciences with humanism. Many observations have been reported on the dehumanization and lack of empathy among medical practitioners. This study aimed to determine empathy among medical students in terms of sex and year level.

Methods This study established the reliability of the 30-item Patient Empathy Scale for Medical Students and compared the empathic attitudes of medical students. A sample of 186 third and fourth year medical students of a private institution was selected as respondents. Data analysis included the estimation of internal consistency using Cronbach's α and factorial ANOVA to determine the influence of sex and year level on the empathy of the medical students.

Results The PESMS had a high reliability coefficient ($r = 0.907$). A significant difference in the empathy scores was confirmed in terms of sex ($P < 0.01$) and year level ($P = 0.01$). However, there was no significant interaction between sex and year level ($P = 0.97$).

Discussion The high reliability coefficient confirmed the consistency or close relation among individual items in the scale and therefore measured an underlying or latent construct of empathy. Analysis provided evidence that a difference in the mean empathy scores existed in terms of sex and year level. However, no interaction between sex and year level was substantiated.

Conclusion: The females displayed more empathic attributes compared to their male counterparts while the third year students were more empathic compared to the fourth year students.

Key words: Empathy, medical education, humanism, scale development

The modern version of the Hippocratic Oath implores physicians to remember that there is art to medicine as well as science, and that warmth, sympathy, and understanding may outweigh the surgeon's knife or the chemist's drug (Webster's New World Medical Dictionary). This statement depicts the import of the humanism of health professionals which includes empathy as an attribute.

Empathy is one of the most highly desirable professional traits that medical education should promote among the students. Larson[1] quoted the dictionary definition of empathy as "the action of understanding, being aware of, being sensitive to, and vicariously experiencing the feelings, thoughts and experience of another without having the feelings, thoughts, and experience fully communicated in an objectively explicit manner." Empathy is a multidimensional construct with cognitive, emotive, and behavioral domains. Cognitive empathy relates to an individual's capacity to understand another person's perspective rather than being exclusively self-oriented, while emotive empathy refers to an individual's tendency to respond to feelings experienced by others.[2] In the field of medicine, empathy is a trait that health professionals are expected to manifest. Rousseau observed that empathy has become a common word in contemporary medicine yet its paucity in clinical application is sadly evident.[3] Such observation of the lack of empathy has

also been perceived among practitioners and students in the local setting. Applicants seeking admission to medical schools are endowed with the idealism of youth, bearing the desire to alleviate the pain of the ill. However, the idealism diminishes or undergoes erosion as the medical student encounters the realities of medical practice, that patient's illnesses and concerns do not always fit the textbook description, more so in the context of the Philippine setting where healthcare is not equitably available to the population. Students end up disillusioned with the realities of the Philippine health situation.

Some experts also argue that it is not possible for a physician to genuinely empathize with every patient—to do so would be emotionally draining and difficult under modern time constraints[3] There are obstacles that prevent the promotion of empathy in medical students; demanding work, little importance attached to empathy and inadequate training in compassion are some of the identified deterrents.[1] The young and malleable psyche of medical students is sensitive to the conditions of the learning environment. Rousseau and Blackburn agreed that the continual mauling of tender young minds by the onslaught of disease and death somehow hardens the soul and in so doing, withers young physicians' awareness of the privileges of medicine and the personhood of patients.[3]

Medical educators should therefore provide avenues for students to mold their empathic attributes. Among these is the availability of role models who embody empathy in their practice of medicine. However, in an era of increased demands on students' time, this will not be easy, but it must be done. There is nothing more treasured than the physician–patient relationship and the personal intimacy a person offers to a physician. This is the essence of medicine—the basis for healing.

Empathy as an expected characteristic of all health care professions cannot be underemphasized. The healing relationship between physicians and patients remains essential to quality care, despite advancement in medical technology.[1]

The promotion of empathy among medical students can lead to patient satisfaction and adherence to treatment plans. Newton maintained that patients view physicians who possess the quality of emotional empathy as being better caregivers.[4] A physician may possess competent diagnostic skills, yet be considered by patients as "ineffective" because the physician misses the link between patient satisfaction, adherence to medical instructions, and physician empathy. The close association between a physician's empathic attributes and the patient's satisfaction cannot be understated. A physician who knows how to relate to and empathize with a patient can have a profound impact on the healing process of a patient. Genuine and heartfelt empathy has many benefits and is associated with trust, which is significantly related to patient outcomes.[3]

The changing topography of the humanistic attitudes of medical students during their training has been dramatically influenced by the rigors of training and the burden of balancing patient care with the advances in and accessibility of modern technology. The physician-patient relationship has become more complicated leading to the detached and uncaring attitudes of the health practitioners.

Empathy is a construct that has been widely discussed and defined differently in literature. In the context of the health professions, several authors have proposed a variety of definitions. Marcus quoted Schafer's definition of empathy as "the ability to understand another person's emotional or life experiences; it is to share those emotions' content but not their intensity.[5] The construct empathy is a predominantly cognitive attribute that involves an understanding of experiences, concerns and perspectives of another person, combined with a capacity to communicate this understanding.[6] Furthermore, empathy is a multistep process that begins with gaining insight into a patient's concerns, feelings and sources of distress.[7]

The current study, however, is founded on the definition of empathy as proposed by Larson and Xiao.[1] The authors adopted the conceptualization of empathy suggested by Davis, defining empathy as a psychological process that encompasses a collection of affective, cognitive and behavioral mechanisms and outcomes in reaction to the observed experiences of another.[1] Cognitive empathy relates to an individual's capacity to understand another person's perspective. Emotive empathy refers to an individual's tendency to respond to feelings experienced by others. Behavioral component involves the outward expression of these internal qualities to influence the patient encounter.

Empathy in the context of clinical care can lead to positive patient outcomes including greater patient satisfaction and compliance, lower rates of malpractice litigation, lower cost of medical care, and lower rate of medical errors.[5] Empathy is one of the most highly desirable professional traits that medical education should promote, because empathic communication skills promote patient satisfaction and adherence to treatment plans while decreasing the likelihood of malpractice suits.[4] The valuing and practice among medical students and practitioners of empathy towards their patients can

impact on the outcomes of their patient – doctor interaction.

The current state of medical education has generated concern on the erosion of students' and residents' humanistic attitudes during their clinical training. Medical educators believe empathy alongside respect and competence to be important components of patient care. This awareness of the impact of empathy has also encouraged medical educators to agree that empathy must be cultivated during medical education and correspondingly assessed.

In the Philippine setting, attitude development and assessment have not been attended to as much as cognitive and psychomotor skills. Several factors may bring about this observation. First, specific learning goals on attitudes are rarely included in the medical curriculum. Without the learning goals, assessment tools for attitudes cannot be developed. Secondly, medical educators have not been adequately trained to observe and assess attitudes.

The aforementioned observations have inspired the development of an attitude scale on empathy. The 30 – item empathy scale can be validated and utilized to further strengthen the development and assessment of empathy among Philippine medical students.

The empathic attributes of selected medical students is further established based on the validated Patient Empathy Scale for Medical Students (PESMS). It is an instrument that measures the empathy of medical students. The information can be used to ascertain when during their education do medical students develop the attributes of empathy. Furthermore, the evidence from the PESMS can be used by medical educators to enhance the medical curriculum particularly on attitude development as empathy. This study aimed to establish the reliability of the 30-item PESMS and compare the levels of empathy of medical students. It also aimed to determine empathy among medical students in terms of sex and year level and to establish the interaction between sex and year level in terms of empathy.

Methods

This two–part descriptive study was conducted in the College of Medicine of a private institution which offers courses in the health sciences. The institution operates a 120-bed hospital that provides health care to both charity and private patients.

A sample of 186 third and fourth year medical students were selected as respondents. In terms of exposure to patients, the fourth year students have more experience in the clinical setting as they spend most of their learning activities in both the pay and charity hospital. The third year students attend to patients assigned to them weekly. Clinical training is interspersed with didactic lectures. The patient encounters are limited to ward visit for 2 to 4 hours weekly.

The 30–item Patient Empathy Scale for Medical Students (PESMS) was developed based on the operational definition of the domains that depict empathy among medical students. It was culled from an initial scale that consisted of sixty statements. A table of specifications (Table 1) was developed to outline the distribution of the affective skills attributed to patient empathy. The PESMS was administered to all 186 participants during the whole month of September 2010 after obtaining approval from the Dean of the College of Medicine. All the participants were asked to agree to and sign an informed consent.

Operationally, empathy was defined as an emotional reaction to another's emotional state or condition that is consistent with the other's state or condition. The construct of empathy encompasses three domains defined as follows: cognitive empathy, the ability to understand another person's perspective; emotive empathy, the ability to respond to feelings experienced

Table 1. Table of specifications of the 30 - item patient empathy scale for medical students.

	Affective Levels					
Major Domains	Receiving	Responding	Valuing	Organization	Characterization	Total
Cognitive Empathy	5	5				10
Emotive Empathy		2	3	5		10
Behavioral Empathy				5	5	10
Total Number of Items/%	5 16.67%	7 23.33%	3 10.00%	10 33.33%	5 16.67%	30 100.00%

by others; and behavioral empathy, the outward expression of these internal qualities.[1]

The data collected were analyzed using IBM SPSS Statistics version 18. The demographic characteristics of the respondents and their responses to the 30 statements in PESMS were encoded. Data analysis included the estimation of internal consistency using Cronbach's a. Factorial ANOVA was used to establish the influence of sex and year level on the empathy of the medical students.

Results

As seen in Table 2, of 186 students included, 53.2% of the respondents belonged to the third year while 46.8% were fourth year medical students. They had a mean age of 24.3 years. The female respondents outnumbered the males 2.5:1.

Table 2. Profile of the third and fourth year medical students (N=186).

	Third Year	Fourth Year		TOTAL
SEX				
Male	26	27		53
Female	73	60		133
	99	87		186
AGE	Mean	SD	Min	Max
Age (Years)	24.3	1.67	21	32

Data were subjected to reliability test using Cronbach's a. The result of the analysis was a reliability coefficient of r = 0.907 compared to 0.912 for standardized 60-item PESMS.

Table 3 depicts the mean empathy scores of the respondents. Values closer to 1.0 indicate high empathy, while values closer to 4.0 depict low empathy. The males had higher scores, indicating lower empathy, compared with the females. The third year medical students exhibited lower mean scores compared to the fourth year students implying that the third year students were more empathic than the fourth year students.

Factorial ANOVA indicated the absence of a significant interaction between sex and year level ($P = 0.97$, $df = 1$). However, there was a significant difference between the female and male medical students in terms of the mean empathy scores ($P < 0.01$). The same difference between the third and fourth year students has also been established scores ($P = 0.01$).

Table 3. Mean empathy scores in terms of sex and year level.

Sex			
Male n = 53		Female n = 133	
Mean	SD	Mean	SD
2.19	0.40	1.94	0.37
Year Level			
Third year n = 99		Fourth Year n = 87	
1.93	0.39	2.10	0.37

Discussion

Analysis of the data indicated a high reliability coefficient of the 30-item PESMS instrument when administered to the sample. A difference in the empathic attributes was also revealed in terms of the sex and year level of the medical students. Moreover, the female students displayed higher empathy compared to the male medical students while the third year medical students possessed higher empathic attributes compared to the fourth year students. However, no significant interaction between sex and year level was detected.

The higher empathy displayed by the females may be due to a biological explanation where women are perceived to be sensitive and caring. The higher empathy displayed by the third year students mirrors the account of Benbassat and Baumal that "humanistic attitudes, such as empathy, decline on repeated measurements as students progress through the medical school curriculum from preclinical training to the clinical clerkships."[7] This account has been reiterated by Newton who tracked the mean scores of 419 students over a four-year period which revealed that student empathy is affected by medical school.[4]

This study suggests that the fourth year medical students were less empathic compared to the younger third year students. This may be attributed to the expanding contact time of the fourth year students with patients. It is surmised that the extended hours watching the pain and suffering of the ill have made students callous and unsympathetic towards their patients. Entry into the clinical environment should provide the opportunity to reinforce empathy development and not bring about its erosion.

The reduction in a student's empathy may burden the patient-physician relationship. Straining the

relationship can diminish the effect of the treatment of disease.

The PESMS was developed as a self-rating instrument of the perceptions of medical students on their empathy. A re-examination of the items is recommended particularly for the statements that were meant to measure behavioral empathy. These items can be inspected and stated to clearly encompass the trait they intend to measure.

The current scale is a self-report of the respondents' perception of empathy. The responses may not indicate the true nature of their empathic attributes. It is therefore suggested that a scale be developed to obtain the patient's appraisal of the empathic behavior of the medical students. After all, the patients are the recipients of the physician's attention and care and are in the best position to articulate whether the medical students exhibit empathy towards them.

A longitudinal cohort or time series study should be carried out to monitor the development or erosion of empathy among medical students and practitioners. Such an endeavor may identify the point in time in which the medical students lost or acquired empathy.

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Comparison of oxycodone iv and fentanyl iv in the attenuation of sympathetic responses to tracheal intubation: a randomized controlled trial

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Abstract

Background This study was undertaken to compare the effect of oxycodone with that of fentanyl in attenuating sympathetic responses induced by tracheal intubation.

Methods Sixty-six ASA physical status I-II patients scheduled for elective surgery requiring general endotracheal anesthesia, were randomly allocated in a blinded fashion to receive an intravenous bolus of either fentanyl 1 mcg/kg or oxycodone 0.1 mg/kg. The systolic blood pressure, diastolic blood pressure, mean arterial pressure and heart rate were measured before induction of anesthesia, before intubation and at 1, 3, 5, and 7 minutes respectively after tracheal intubation.

Results There were statistically significant differences in the results of blood pressures and heart rate in both groups indicating sympathetic response during laryngoscopy and tracheal intubation. However, blood pressures and heart rates significantly increased in Group F compared with those of Group O.

Conclusion Oxycodone caused less variation in arterial pressures and increases in heart rate than fentanyl. It can provide an effective control of the inotropic response induced by laryngoscopy and tracheal intubation.

Key words: Tracheal intubation, sympathetic response, oxycodone

Manipulation of the airway, particularly direct laryngoscopy and endotracheal tube intubation following the induction of anesthesia frequently produces hemodynamic instability mediated by sympathetic efferents via the cardioaccelerator nerves and sympathetic chain ganglia. This results in a diffuse autonomic response that includes widespread release of norepinephrine from adrenergic nerve terminals and the secretion of epinephrine from the adrenal medulla leading to hypertension, tachycardia and increased oxygen consumption. These hemodynamic changes may produce serious complications especially in patients with underlying abnormalities causing increased intracranial pressure, herniation and myocardial infarction.[1]

These hemodynamic changes are inevitable, and therefore the addition of opioids is widely used to supplement the induction of general endotracheal anesthesia. Opioids act on stereospecific opioid mu, delta and kappa receptors. They are coupled to G proteins and inhibit adenylate cyclase, thereby decreasing the conduction of voltage-gated calcium channels. Any of these effects will result in decreased neuronal activity, preventing increases in blood pressure, heart rate and oxygen consumption.[2]

Fentanyl is one of the most commonly used opioids during induction of general anesthesia. It is administered as an adjuvant to inhaled anesthetics in an attempt to blunt circulatory responses during intubation of the

trachea. It is a phenylpiperidine-derivative opioid agonist that has a rapid onset and shorter duration of action than morphine. Despite the impression that fentanyl produces rapid onset of action, EEG tracings show that there is a distinct time lag between the peak plasma concentrations of fentanyl. This delay reflects the effect site equilibration time between the blood and the brain which is estimated to be 6.4 minutes. As an analgesic, fentanyl is 75 to 125 times more potent than morphine.[2]

Oxycodone is a semisynthetic opioid that exerts an agonistic activity on mu, kappa and delta receptors. Equivalence with morphine is 1:1.[3] Oxycodone has the same mechanism of action as other opioids. Most of the drug is metabolized in the liver, while the rest is excreted in the kidney along with its metabolites. The two main metabolites are oxymorphone, a very potent analgesic and noroxycodone, a weak analgesic.[4] Compared to fentanyl, both are synthetic pure opioid agonists.

No studies or literature comparing the hemodynamic changes during the induction of general endotracheal anesthesia using oxycodone or fentanyl have been found. The purpose of this study was to compare the effect of oxycodone with that of fentanyl on hemodynamic stability, as well as the undesirable effects, when used as an opioid supplement during direct laryngoscopy and tracheal intubation. Specifically, it aimed to compare the efficacy of oxycodone with fentanyl in preventing sympathetic response using the following parameters: blood pressure, heart rate, oxygen saturation and adverse effects.

Methods

This was a randomized double blind controlled trial. This study was approved by the technical and ethical review committees of the institution.

Both male and female patients, classified under ASA Risk I and II aged 18 to 60 years, scheduled for elective general surgery for which tracheal intubation was indicated were recruited. A written informed consent was obtained. Patients with known hypersensitivity to opioids, oxycodone or any of the other constituents, or in any situation where opioids are contraindicated; head injury; paralytic ileus; COPD; bronchial asthma; moderate to severe hepatic impairment; severe renal impairment; concurrent administration with MAO inhibitors; pregnancy and lactation were excluded.

A sample size of 33 subjects per group was calculated with an 80% power and an alpha of 0.05. A 20% change in the blood pressure of was considered significant. This calculation is also based on the assumption that the standard deviation of the independent variable is 2.6 mmHg[5], which yielded 28 subjects per group. Another 5 subjects per group were added to compensate for dropouts.

Patients were allocated by block randomization to either oxycodone (Group O) or fentanyl (Group F) groups based a computer-generated set of random numbers in sealed opaque envelopes. Syringes containing oxycodone or fentanyl were prepared by a collaborator not involved in the study procedure. The contents of each syringe were diluted with normal saline solution to make a volume of 5 cc. The collaborator administered the drug while a blinded observer collected the data and a blinded anesthesiologist intubated the patient.

Premedication with midazolam 0.05 mg/kg IV was given at the wards prior to transfer to the operating room. Upon entering the operating room, each patient was monitored in a non-invasive manner for blood pressure (NIBP), heart rate (HR), electrocardiogram (ECG), and partial oxygen saturation (SpO_2). Pre-induction measurements of systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure (MAP), heart rate (HR) and partial oxygen saturation (SpO_2) were used as baseline values.

Patients received either oxycodone IV 0.1 mg/kg (Group O) or fentanyl 1 mcg/kg (Group F) upon induction. These doses are equipotent with 0.1 mg/kg of morphine IV.[3] Propofol 1-2 mg/kg IV was given 1 minute later. Patients were ventilated with 100% oxygen and sevoflurane MAC-BAR (2.7%). Atracurium 0.6 mg/kg was used as neuromuscular blocker. Orotracheal intubation was performed after five minutes. Direct laryngoscopy was carried out with the use of a Macintosh blade 3 or 4 at peak effects of IV fentanyl or IV oxycodone, and tracheal intubation was accomplished with Murphy endotracheal tube, with a maximum of 2 attempts. Patients not intubated within 2 attempts were dropped from the study, but was still considered in the data analysis. The patients' lungs were mechanically ventilated with a tidal volume of 8 ml/kg and a respiratory rate of 12/min to maintain end-tidal $PaCO_2$ of 35 to 45 mmHg. Anesthesia was maintained with sevoflurane.

The demographic characteristics such as age, sex, ASA risk, weight (kg), height (cm), induction time (sec), duration of laryngoscopy (sec) were recorded. Co-morbidities such as hypertension, diabetes mellitus, smoking, heart disease, renal disease and intake of anti-hypertensive medications, use of beta agonists were likewise noted.

The hemodynamic response to laryngoscopy and intubation was assessed through blood pressure (systolic, diastolic, mean arterial pressure), heart rate, and SpO_2

measured at three time-points: baseline (30 minutes after giving midazolam), preintubation (6 minutes after treatment), and post intubation (at 1, 3, 5, and 7 minutes after intubation). Adverse events such as hypotension, bradycardia, increased intracranial pressure, herniation, myocardial infarction during the study period were also noted.

The demographic data were analyzed using unpaired t-test, Mann Whitney U or Fisher's exact test. The mean of the blood pressure, heart rate and oxygen saturation were calculated accordingly. These were analyzed using the Student's t-test. Ordinal variables were presented as numbers (%). A value of $P<0.05$ was considered statistically significant. IBM™ SPSS Statistics Version 20 Program was used for the analysis of the results.

Results

Of the 66 patients included in the study, 63 completed the protocol. The three patients who did not complete the study were dropped, but were later used in the intention-to-treat analysis. One subject exceeded the number of laryngoscopy attempts described by the study, i.e., three attempts requiring the aid of an Eshman. Another developed rashes and was given diphenhydramine 50mg IV; they subsided after a few minutes and the operation proceeded without any other complications. This patient has had allergic reactions to several different medications, but it could not be determined whether or not the rashes were due to the treatment drug. Another subject was given rocuronium instead of atracurium, which violated the study protocol. The intention-to-treat analysis showed that the drop-outs had no effect in the results of the study.

There were no demographic differences between the two groups as seen in Table 1. There was also no significant difference between the Mallampati and Cormack-Lehane grades of the two groups.

The preoperative arterial pressure, systolic, diastolic, mean arterial pressures were not significantly different between the two groups. Preoperative heart rates, though, were significantly different. This was treated statistically using standardization in the analysis. There were significant differences in sympathetic response during laryngoscopy and tracheal intubation between the two groups as shown in the measurements of blood pressure (Figures 1-3) and heart rate (Figure 4). The standardized heart rate was significantly increased at 1, 3, 5 and 7 minutes after intubation in Group F compared with Group O (Figure 4). Likewise, the results showed that the blood pressure readings 1, 3, 5 and 7 minutes after intubation were significantly different between the two groups (Figures 1-3). The differences in the results indicate that Group O had significantly lower blood pressure and standardized heart rates than those in Group F (Figures 1-4). It is also interesting to note that the mean heart rates just before intubation were the same in both groups, despite having different baseline levels.

Table 1. Demographic characteristics and peri-intubation measured data of patients (Mean±SEM or Number).

	Group F (Fentanyl)	Group O (Oxycodone)	P-value
No. of Patients	32	31	
Age (years)	42.84	39.13	0.269
Sex (Male/Female)	10/22	9/22	0.848
ASA (I/II)	8/24	9/22	0.718
Weight (kg)	58.78±1.90	58.97±2.45	0.952
Height (cm)	158.53±1.64	158.97±1.40	0.841
BMI (kg/m^2)	23.34±0.60	23.25±0.83	0.930
Duration of Laryngoscopy (sec)	25.31±1.33	25.48±1.51	0.932
Mallampati (1/2/3/4)	17/12/2/1	23/5/3/0	0.174
Cormack-Lehane (1/2/3)	15/16/1	18/13/0	0.457

No significant difference among groups.

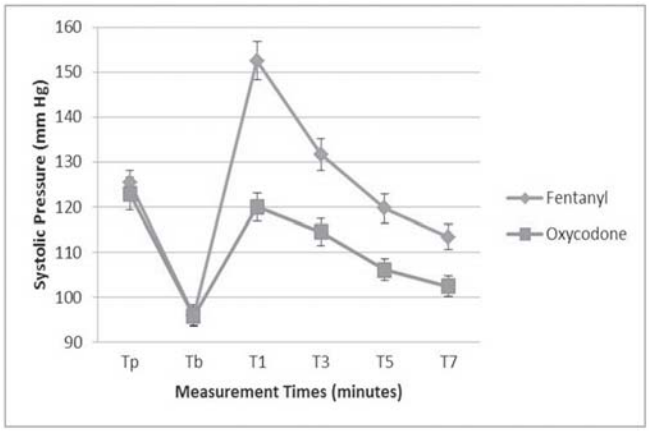

Figure 1. Changes in systolic blood pressure during intubation in the fentanyl and oxycodone groups.

Data are mean ± SD ◆ = Group F (Fentanyl); ■ = Group O (Oxycodone); Tp = baseline; Tb = before intubation; T1, T3, T5, T7 = 1, 3, 5, 7 minutes after intubation respectively.

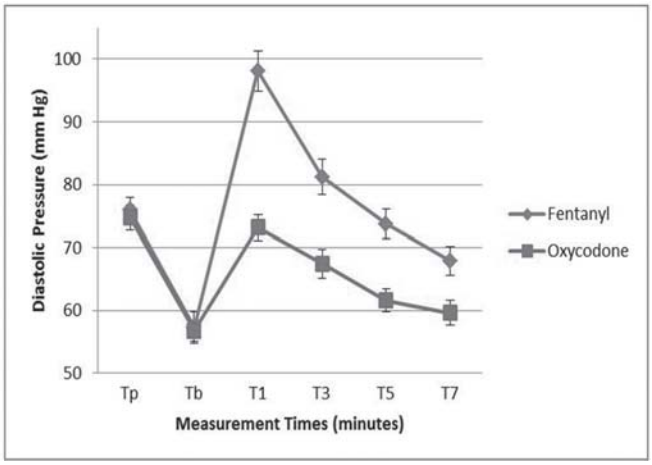

Figure 2. Changes in diastolic blood pressure during intubation in the fentanyl and oxycodone groups.

Data are mean ± SD ◆ = Group F (Fentanyl); ■ = Group O (Oxycodone); Tp = baseline; Tb = before intubation; T1, T3, T5, T7 = 1, 3, 5, 7 minutes after intubation respectively.

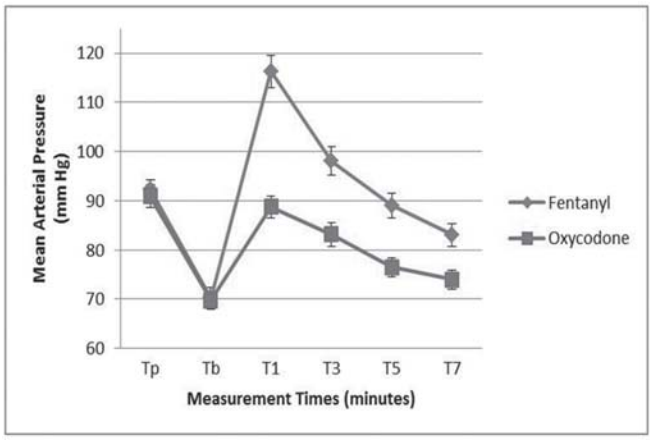

Figure 3. Changes in mean arterial pressure during intubation in the fentanyl and oxycodone groups.

Data are mean ± SD ◆ = Group F (Fentanyl); ■ = Group O (Oxycodone); Tp = baseline; Tb = before intubation; T1, T3, T5, T7 = 1, 3, 5, 7 minutes after intubation respectively.

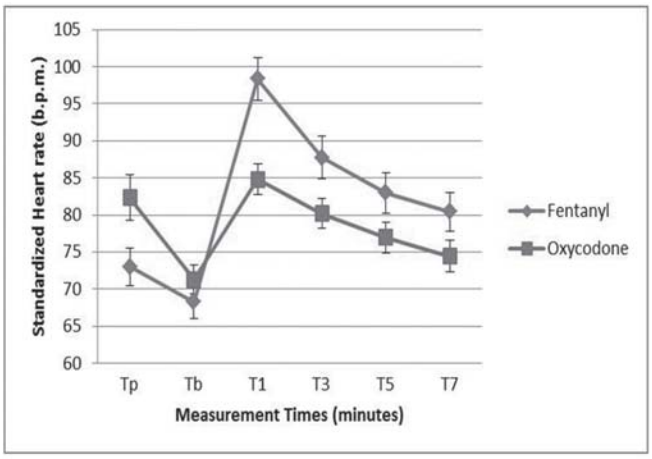

Figure 4. Standardized heart rate during intubation in the fentanyl and oxycodone groups.

Data are mean ± SD ◆ = Group F (Fentanyl); ■ = Group O (Oxycodone); Tp = baseline; Tb = before intubation; T1, T3, T5, T7 = 1, 3, 5, 7 minutes after intubation respectively.

The oxygen saturation was maintained at 99-100% in all subjects throughout the study period. There were no cases of hypotension, bradycardia, increased intracranial pressure, herniation or myocardial infarction in either group.

Discussion

This study compared the efficacy of fentanyl 1 mcg/kg IV and oxycodone 0.1 mg/kg IV in controlling the sympathetic responses to tracheal intubation. The results showed that oxycodone was able to attenuate the increases in systolic, diastolic, mean arterial pressure and heart rate after tracheal intubation better than fentanyl.

Surgical procedures requiring general anesthesia often involve interventions such as direct laryngoscopy and tracheal intubation. The manipulation in the larynx and trachea causes the release of catecholamines resulting in various sympathetic responses including

tachycardia, hypertension and elevated total oxygen consumption.[1] These reflex changes lead to an average increase in blood pressure by 40%-50% and increase in heart rate by 20%.[6] Significant elevations of circulating norepinephrine and epinephrine following laryngoscopy with or without tracheal intubation have been found in several studies.[7,8] Therefore the prevention of sympathetic activity may prove particularly beneficial especially to patients with limited cardiac reserve.[9]

At present, different pharmacologic agents are used to prevent sympathetic response to tracheal intubation, including beta blockers[10], calcium channel blockers[11], vasodilators[12], IV lidocaine[13], and alpha 2 agonists.[14] Opioids, in moderate to high doses have been suggested as a means of blunting this response.[15] In a study done by Ko, the use of a small dose fentanyl and its optimal time of administration proved to be effective in blunting the circulatory responses to tracheal intubation in healthy normotensive patients.[16]

Oxycodone is currently used for the treatment of moderate to severe pain in patients with cancer and postoperative pain. It is a full opioid agonist with no antagonist properties. It has an affinity for kappa, mu and delta opioid receptors in the brain and spinal cord. Oxycodone is similar to morphine in its action. The therapeutic effect is mainly analgesic, anxiolytic, antitussive and sedative. Side effects are also common with the use of opioids, although oxycodone causes less nausea, hallucinations and pruritus than morphine.[3] Fentanyl on the other hand, is a synthetic opioid agonist similar to morphine. It is widely administered as an adjuvant to inhaled anesthetics in an attempt to blunt circulatory responses to tracheal intubation or sudden changes in the level of surgical stimulation. It has an advantage of stable hemodynamics due to the lack of direct myocardial depressant effect, absence of histamine release and suppression of the stress response to surgery. Disadvantages include persistent or recurrent depression of ventilation which is a potential postoperative problem.[2]

A study by Ko demonstrated that when small doses of opioids are used before tracheal intubation, the timing of administration must be taken into consideration in order to maximize the advantages. Fentanyl has an immediate onset of action, 5 to 8 minutes after its administration. [16] On the other hand, oxycodone has an onset of action between 5 to 10 minutes after IV administration. In our study, both opioids were given 7 minutes prior to laryngoscopy and tracheal intubation.

This study revealed that when compared to fentanyl, oxycodone causes less hemodynamic variations during laryngoscopy and tracheal intubation. Both groups developed tachycardia and hypertension during larygoscopy and tracheal intubation indicating a reflex sympathetic reaction to the mechanical stimulation of larynx and trachea. However, tachycardia and increases in systolic, diastolic and mean arterial pressure were significantly more in patients receiving fentanyl.

The results of our study suggest a beneficial effect of oxycodone on hemodynamic and sympathetic outflow changes in the induction of anesthesia. It revealed that oxycodone is more effective than fentanyl in suppressing sympathetic outflow at a dose of 0.1 mg/kg IV given 7 minutes before direct laryngoscopy and tracheal intubation, thereby blocking catecholamine release and the subsequent hemodynamic changes that occur during the manipulation of the airway. Oxycodone caused less variation in arterial pressures and increases in heart rate than fentanyl. There were no adverse events encountered in the study, such as hypotension, bradycardia, increased intracranial pressure, herniation or myocardial infarction in either group.

The proponents of this study recommend the use of oxycodone at a dose of 0.1 mg/kg, 7 minutes prior to laryngoscopy as an adjunct for the induction of general anesthesia. It provides an effective control of the inotropic response brought about by direct laryngoscopy and tracheal intubation. It is also recommended that a follow-up study be done to determine the cost-effectiveness of oxycodone for the attenuation of the hemodynamic changes during tracheal intubation.

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EEG findings in infarcts and hemorrhagic post-stroke seizures: A cross-sectional study

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Abstract

Background There is a paucity of literature dealing with post-stroke seizure EEG abnormalities and perhaps none that compares them between infarcts and hemorrhagic strokes. In this study, we aimed to find out whether EEG abnormalities were associated with the type, location and interval of stroke.

Methods In this cross-sectional study from 2008 to 2012, the EEG findings (normal, abnormal significance I-III) of post-stroke patients who had seizures were compared with the type (infarct or hemorrhage) and location (cortical, subcortical, brainstem or cerebellar) of stroke, and with the interval of stroke ictus to EEG. The location was based on neuro-imaging studies; other data were retrieved from the EEG requests and clinical records of the patients.

Results Ninety-eight patients with a mean age of 63.9 years, majority of which were females, who had infarcts, and had abnormal EEG findings, were included. Hemorrhagic strokes were significantly associated with more severe abnormalities (abnormal significance III) on EEG (P = 0.04). The location of the stroke did not show any statistically significant correlation with EEG abnormalities in our study. The time elapsed between stroke and the EEG was not significant (P = 0.09).

Conclusion The most common EEG abnormality seen on in the EEGs of post-stroke patients was intermittent focal or generalized slowing of the background and most severe EEG abnormalities were noted on EEGs of hemorrhagic stroke patients rather than infarctions. In this study, the EEG abnormality did not appear to correlate well with the location of the stroke.

Key words: electroencephalogram, stroke, infarct

There is a paucity of literature regarding the correlation of abnormalities on the electroencephalogram (EEG) and post-stroke seizures. Most of the available literature deals with risk factors for developing seizures after the occurrence of stroke, but these studies rarely delve into the correlation between the seizures and the EEG findings in these patients. A retrospective study by Gupta, et al.[1] revealed that the most common EEG findings were focal slowing of the background over the area affected by the infarction. A prospective study by Dhanuka, et al.[2] found that a cortical lesion was associated with a higher risk of developing seizures. They found that half of patients had normal EEGs; 26% had diffuse slowing; 22% had focal slowing; and 17% had epileptiform discharges. However, contrary to findings in Western literature, the time of seizure onset (acute, early or late phase) did not correlate with the development of epilepsy.

A local study in 2009 on the risk factors for the development of post-stroke seizures found that post-stroke seizures occurred in 5.9% of the patients followed up for two years. A third of the patients had EEGs available for review. Seizures occurred most frequently in cortical, combined cortical and subcortical lesions, and in subarachnoid hemorrhage. The findings were focal slowing over the area affected by the stroke (36%); generalized slowing of the background (27%); and epileptiform discharges (27%).

Patients who had recurrent strokes had higher seizure occurrence rates.[3]

To our knowledge, ours is the first local study that reviewed a large number of EEGs in post-stroke patients.

Our aim was to find out whether:

1. EEG abnormalities were more likely to occur in infarcts or hemorrhages;
2. These EEG abnormalities are more severe in infarcts or hemorrhages;
3. The location of the stroke has an effect on the abnormality seen on EEG; and
4. The interval between stroke (ictus) and EEG affected the degree of abnormality.

Methods

This cross-sectional study done at the University of the East Ramon Magsaysay Memorial Medical Center involved post-stroke patients who had seizures. Their EEG findings were correlated with the results of neuro-imaging studies.

The EEGs of post-stroke patients done at the Neurophysiology Laboratory were identified and retrieved. The results of neuro-imaging studies and clinical data were obtained from their respective EEG requests or from the Radiology Section. When necessary, charts of patients who were admitted in the hospital were reviewed. Patients who had concomitant encephalopathy (metabolic, toxic, septic, hepatic or uremic) and intracranial tumors were excluded. The following data were extracted: patient demographics, EEG findings, type and location of stroke, and interval between stroke ictus and EEG.

EEG findings were reported as: normal, abnormal significance I (mild), abnormal significance II (moderate) or abnormal significance III (severe). Their definitions are seen in Table 1. Type of stroke was either infarction or hemorrhage (intraparenchymal, subarachnoid, ruptured arteriovenous malformation). Based on location, strokes were classified as cortical (frontal, parietal, temporal and occipital); subcortical (corona radiata, periventricular white matter, basal ganglia, thalamus, internal capsule); brainstem (midbrain, pons and medulla); or cerebellar. In instances where multiple foci were noted on imaging, the most prominent and/or most recent lesion was considered as the location of the stroke. All neuro-imaging studies were interpreted by board-certified radiologists. The official results were used in this study.

The data were then encoded and analyzed using SPSS version 10 for Windows. Descriptive statistics were generated for all variables. For nominal data, frequencies and percentages were computed. For numerical data, means ± standard deviations (SD) were generated. Analysis of variance (ANOVA) was used to determine the association of the time interval between the stroke ictus and the EEG when the abnormality was noted. Chi-square test was used to determine the association between type of stroke and degree of EEG abnormality, and location of stroke and EEG abnormality.

Results

There were 125 EEGs done on post-stroke patients from January 2008 to June 2010. Of these, 27 had no neuro-imaging studies and/or clinical data, leaving 98 for inclusion in the study. The subjects had a mean age of 63.9 years, and included a baby and two adolescent males. Majority of the subjects were women and had infarctions. More than 80% of subjects had abnormal EEG findings, of which 40% were classified as abnormal significance II. Table 2 shows the distribution of patients according to age, sex, type of stroke and EEG findings.

Table 3 shows a significant association between the type of stroke and the degree of abnormality on EEG ($P = 0.04$, Chi-square). All patients with hemorrhagic stroke had abnormal EEG findings while only 80% of those patients with infarction had abnormal EEGs.

Table 1. Cleveland Clinic EEG Classification (1970).

EEG Classification	
Normal	
Abnormal Significance I (MILD)	Generalized slowing of the background
Abnormal Significance II (MODERATE)	Intermittent generalized or focal slowing of the background
Abnormal Significance III (SEVERE)	Continuous focal or generalized slowing of the background and/or presence of epileptiform discharges

Table 2. Demographic characteristics of subjects (N = 98).

Characteristics	Frequency	Percentage
Age in years		
≤10	1	1.0
11 - 20	3	3.0
21 - 30	7	7.1
31 - 40	3	3.0
41 - 50	5	5.1
51 - 60	18	18.4
61 - 70	17	17.3
71 - 80	21	21.4
81 - 90	17	17.3
>90	6	6.1
Mean ± SD = 63.9 ± 21.1		
Sex		
Female	54	55.1
Male	44	44.9
Type of Stroke		
Infarction	82	83.7
Hemorrhage	16	16.3
EEG Results		
Abnormal I	20	20.4
Abnormal II	39	39.8
Abnormal III	23	23.5
Normal	16	16.3

Around 60% of patients with infarcts had abnormal significance I or II EEG findings while more than 85% of hemorrhagic stroke patients had abnormal significance II or III EEGs. Among the 23 patients who had abnormal significance III EEG results, 14 had epileptiform discharges. Eight patients had infarcts (7 cortical, 1 subcortical) and the other six had hemorrhage (1 cortical, 5 subcortical). Epileptiform discharges occurred in 37.5% of hemorrhagic stroke patients and in less than 10% of infarct patients. These epileptiform discharges occurred focally over the area affected by the stroke in 13 patients while the remaining patient had generalized epileptiform discharges. She had suffered from a right parieto-occipital bleed with intraventricular extension.

Table 4 shows no significant association noted between the location of the stroke and abnormal findings on EEG (P = 0.72). Nine out of 10 patients had cortical or subcortical strokes. Almost 90% of patients with cortical lesions had abnormal EEGs compared with three-fourths in patients with subcortical lesions.

Table 5 shows no significant association between the time elapsed from stroke ictus and the degree of abnormality on EEG (P = 0.09, ANOVA). However, more severe EEG abnormalities were noted within 2-5 years from the ictus of the stroke. EEGs done 5 years after stroke tended to be normal. Three of 14 patients with epileptiform discharges had their EEGs done in the acute phase of their stroke (within 72 hours of the ictus). Two of these patients had hemorrhage, one had an infarction. The remaining 11 patients had their EEGs done between 1-22 years after the stroke, with a mean interval of 4 years between the stroke ictus and EEG recording.

Discussion

Population studies by Hauser[5] revealed that stroke is the most common cause of epilepsy in adults. The prevalence of seizures occurring after stroke is 5-48%.[2,4] Factors consistently identified with post-stroke seizures are cortical location of the stroke[2, 4, 6,7], hemorrhage[7, 8] or *severe* ischemic stroke.[4,6,8,9] Early seizure occurrence, during the acute phase of the stroke (≤ 72 hours) or

Table 3. Association of type of stroke with EEG results.

	EEG Results Abnormal III (N=23)	Abnormal II (N=39)	Abnormal I (N=20)	Normal (N=16)	Total
Type of Stroke					
Infarction	16 (19.5%)	32 (39.0%)	18 (22.0%)	16 (19.%)	82
Hemorrhage (Bleed)	7 (43.8%)	7 (43.8%)	2 (12.5%)	0	16

P = 0.04 (chi-square test)

Table 4. Association of location of stroke with EEG results.

	EEG Results Abnormal III (N=23)	Abnormal II (N=39)	Abnormal I (N=20)	Normal (N=16)	Total
Location of Stroke					
Brainstem	0	1 (50.0%)	1 (50.0%)	0	2
Cerebellar	1 (50.0%)	0	0	1 (50.0%)	2
Cortical	15 (24.2%)	25 (40.3%)	14 (22.6%)	8 (12.9%)	62
Subcortical	7 (23.3%)	12 (40.0%)	4 (13.3%)	7 (23.3%)	30
No definite location	0	1 (50.0%)	1 (50.0%)	0	2

P = 0.72 (chi-square)

Table 5. Association between time elapsed (in years) from ictus and EEG results.

	EEG Results Abnormal III (N=23)	Abnormal II (N=39)	Abnormal I (N=20)	Normal (N=16)
Time in Years				
Mean ± SD	2.89 ± 4.96	2.50 ± 3.54	4.28 ± 4.68	5.12 ± 5.58

P = 0.09 (ANOVA)

within 2 weeks after the ictus was more common in large infarcts.[1,2,6] These early onset seizures did not persist beyond a few months.[6, 8, 9] Many studies have suggested that hemorrhage[7,8] increases the risk of post-stroke seizures, although some authors claim that infarction poses a higher risk for seizures.[6, 9]

Our data are consistent with those obtained from the scarce amount of literature[1,2] in terms of EEG abnormalities in post-stroke seizures. More than 80% had infarctions, with abnormal significance II EEGs - intermittent focal or generalized slowing of the background – being the most common finding. The EEG findings of the other infarct patients were almost evenly distributed across the remaining categories. All patients who had hemorrhagic stroke had abnormal EEGs, with more than 80% having severe changes (abnormal significance II-III). This corroborates findings from literature that hemorrhagic stroke patients are more at risk for developing post-stroke seizures than patients who had infarctions.[7, 8]

A third of the patients had severe EEG abnormalities and two-thirds of them had epileptiform discharges. The stroke type did not appear to be associated with the likelihood of finding epileptiform discharges on EEG since the patients were almost evenly distributed across the two stroke subtypes (6 hemorrhages and 8 infarctions). This may be due to the small number of hemorrhagic stroke patients. On the other hand, our study showed that most of the patients who had hemorrhagic stroke and epileptiform discharges had a *subcortical* rather than a cortical location of the stroke, contrary to the literature review.[2,4,6,7] Patients with infarctions and epileptiform discharges had a relatively large stroke in the cortical area.

Contrary to the literature, the authors did not find an association between location of the stroke and abnormal EEGs findings although the data indicate that at least 75% of patients with cortical or subcortical lesions had abnormal EEG findings.

The data showed that when an EEG was done within 2-5 years of the ictus, the likelihood of seeing an abnormality was higher. EEGs with abnormal significance II-III were seen around 2 ½ years after the stroke while normal EEGs were seen after five years. This raises the question whether or not patients at risk for post-stroke seizures (i.e., hemorrhagic stroke patients) should undergo EEG for screening during the course of their illness and recovery.

To the authors' knowledge, this is the first study to review a relatively large number of EEGs in post-stroke patients with seizures. The literature cited had 11-35 EEGs. This is also the first local study correlating EEG

findings with the type of stroke, location, and interval between ictus and EEG. This study showed that hemorrhagic stroke patients had more severe abnormalities on EEG when compared to infarct patients. There was a tendency for abnormal EEGs to be seen within five years of the stroke. The location of the stroke did not appear to correlate with the degree of abnormality seen on EEG. We recommend a reevaluation of the association of these parameters when more EEGs are accrued.

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Comparison of laryngoscopic view and ease of intubation with the use of Truview EVO2™ System (Truphatek®), and Macintosh blade in adult patients with predicted difficult intubation

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Abstract

Introduction The timely management of a difficult airway is a critical skill for any anesthesiologist. This includes proficiency in the use of different devices to aid in securing the airway. One such device is the Truview EVO2 laryngoscope as an alternative to the conventional laryngoscope to intubate patients with anticipated or unrecognized difficult airway.

Methods This study compared the Cormack-Lehane laryngoscopic view and ease of intubation in forty patients randomized to be intubated using the Truview EVO2 or the Macintosh blade. Changes in mean arterial pressure and heart rate were also noted.

Results Patients intubated with the Truview had a significantly better laryngoscopic view, fewer attempts to put in the tube, and shorter time to successful intubation. Subjects in this group were also noted to have lower mean arterial pressure after intubation.

Conclusion The Truview laryngoscope afforded better laryngoscopic view and optimal conditions for intubation in patients predicted to have difficult airways. The reduced hemodynamic stimulation also presented an added benefit.

Key words: Laryngoscopic view, intubation, difficult intubation, Macintosh blade, Truview EVO2.

Safe perioperative care necessitates successful airway management. Although infrequent, difficult intubation may lead to morbidity or even mortality. Based on available data the incidence of difficult intubation is 4.5% to 7.5%, whereas the incidence of failed intubation is 0.01% to 0.03%.[1] According to the American Society of Anesthesiologists (ASA) closed claims database from 1990 to 2007, 31-32% of claims had death and brain damage as outcome. This was caused by adverse respiratory events in 45% of cases - attributable to inadequate ventilation in 7%, esophageal intubation in 7%, and difficult intubation in 12%.[2]

Several airway devices and equipment have been developed over the years to aid anesthesiologists in these situations. Videolaryngoscopes and fiberoptic bronchoscopes provide indirect visualization of the glottis, with the latter involving a steeper learning curve. The Truview EVO2 on the other hand is an optical laryngoscope used like a conventional laryngoscope. It has a slim, straight laryngoscope blade that has a tip curved 40 degrees upward. The proximal blade is fitted with a telescope that can be viewed with the naked eye or an endoscopic camera head. A lateral port may be connected to an oxygen source to prevent misting and provides a continuous oxygen source during intubation.[1,3] According to Barak, Truview offers a better laryngoscopic view with lesser maximal force and fewer soft tissue injuries when compared with the Macintosh blade. However, the duration of intubation was longer.[3] Matsumoto also reports of two cases of failed intubation with Macintosh blade that were successfully intubated using the Truview.[4]

This study aimed to compare the ease of laryngoscopy and intubation using the Truview blade with the conventional Macintosh (Mac) Blade in patients with predicted difficult airways, specifically:

1. To compare the Cormack-Lehane grades attained using the Truview EVO2 laryngoscope or Macintosh blade.
2. To compare the number of attempts needed to successfully intubate patients with difficult airway using either the Truview or Macintosh blades.
3. To compare the hemodynamic changes that occur with intubation using the Truview or Macintosh blades.

Methods

All patients scheduled to undergo elective surgery under general endotracheal anesthesia with predicted difficult airway were included in the study after obtaining informed consent. Airway evaluation was done using the Simplified Predictive Intubation Difficulty Score (SPIDS).[5] This predictive scoring system was found to have 65% sensitivity, 76% specificity, 14% positive predictive value, and 97% negative predictive value. Patients with SPIDS score greater than 10 were considered to have difficult airways.

Sample size was calculated at 80% power, 0.05 α error and effect size of 20. This yielded 18 for each but a total of 40 subjects were enrolled, with 20 subjects per group to allow for drop-outs.

The subjects were randomized into group A (Macintosh blade) and group B (Truview blade) using a computer-generated table of random numbers. Patients were placed on NPO for 8 hours, with no premedication given. At the operating room, standard monitors (BP, pulse oximeter, ECG and capnograph) were attached and baseline vital signs were automatically recorded in the monitoring device. Patients were pre-oxygenated for five minutes after which general anesthesia was induced with midazolam, propofol, fentanyl and atracurium, computed based on weight and adjusted for age and body mass index (BMI).

Intubation was attempted using either a Truview or Mac blade after disappearance of single twitch on peripheral nerve stimulator. The endotracheal tubes used were appropriately sized for gender (7.0–7.5 for females and 7.5–8.0 for males). Two experienced anesthesiologists equally adept with use of Macintosh blade and with more than 10 successful Truview intubations performed the intubations of all the subjects. An assistant timed laryngoscopy - time from the insertion of the blade to successful intubation in seconds was "time to intubation" (Ti). The number of attempts before a successful intubation was also counted and recorded for each patient. Correct placement of the tube was verified by capnography and auscultation. The intubator scored the laryngoscopic view using the Cormack-Lehane grading system.

The monitoring device automatically recorded vital signs of patients - prior to laryngoscopy, at the start of laryngoscopy, and 1 minute after successful intubation. The maintenance of anesthesia was left to the discretion of the attending anesthesiologist.

Statistical analysis was done using SPSS Statistics Data Editor v. 17.0. Nominal data were analyzed using the Chi-square test, ordinal data with Kruskal-Wallis test, comparison of means with the t-test, and pairwise comparison of hemodynamic parameters with the Bonferroni test. P value was set at 0.05.

Approval for the study was obtained from the hospital research ethics committee.

Results

Forty patients were recruited and randomized into two groups. Table 1 shows no significant difference between the two groups. Table 2 shows the comparison of intubation conditions and laryngoscopic views obtained using the Macintosh and Truview blades. The time to intubate was significantly shorter with the Truview blade. The number of attempts to successfully intubate with Truview was significantly fewer than that of the Macintosh. There was no failure to intubate in both groups. The Cormack-Lehane grading showed significantly better laryngygoscopic views with Truview. More subjects in the Truview group were given Cormack-Lehane grades of 1-2, meaning easy intubations or optimal laryngoscopic views. There were fewer subjects in the Truview group who received Cormack-Lehane scores of 3-4, indicative of poorer laryngoscopic views.

Table 3 shows the analysis of variance in the hemodynamic parameters between groups. The mean arterial pressures after intubation in the Truview subjects were significantly lower. There was no difference in the mean heart rate between the two groups. Tables 4 and 5 show the pairwise comparison of mean arterial pressure (MAP) and heart rate, respectively, within the Macintosh and Truview groups. As seen in Table 4, there were significant differences in the MAP of patients within the respective groups between baseline and during intubation, as well as during and after intubation. The baseline and post-intubation MAPs were comparable.

Table 1. Comparison of patient characteristics between Macintosh and Truview groups.

	Macintosh	Truview	P value
Mean Age (SD)	54.5 ±15.0	50.0 ±12.3	0.213[a]
Sex			
Male	8	10	0.75[b]
Female	12	10	
Mean BMI (SD)	26.2 ± 5.9	34.7 ±17.6	0.051[a]
Mouth opening			
> 3.5 cm	20	20	
Thyromental distance			
> 6cm	15	15	
<6 cm	5	5	
Neck Mobility			
Full	18	12	0.065[b]
Restricted	2	8	
Mallampati			
I	0	2	0.294[c]
II	4	5	
III	12	12	
IV	4	2	

[a]t-test, [b]chi-square test, [c]Kruskal-Wallis test

Table 2. Comparison of laryngoscopy and intubation between Macintosh and Truview groups.

	Macintosh	Truview	P value
Time to intubate (secs)	17.6 (4.5)	14.8 (2.7)	0.023[a]
Number of attempts			
1	10	16	0.033[b]
2-3	7	4	
>3	3	0	
Cormack-Lehane Grading			
I	3	6	0.018[b]
II	5	10	
III	7	3	
IV	5	1	

[a]t-test, [b]Kruskal-Wallis test

A significant difference in heart rate was noted between baseline and during intubation for both Macintosh and Truview groups. The changes in baseline, pre- and post-intubation heart rates for both groups were comparable as seen in Table 5.

Discussion

The Truview blade was designed with a 40±2 degree angled deflection view of the vocal cords through a 15-mm eyepiece.[6] The prism effect provided improved visualization of structures in an anteriorly positioned glottis where a traditional laryngoscope like a Macintosh blade would give a poor view. This study showed significantly better Cormack-Lehane grades with Truview than with Macintosh. This corroborated the findings of improved glottic views that provided optimal intubating conditions.[4,6,7]

This study's findings of shorter intubation times with Truview contrasted with that of Barack.[3] The difference may be because there were only two intubators in this study, minimizing operator variability. In addition, the proficiency of the intubators with Truview use may have played a role. Likewise, successful intubation was achieved with fewer attempts when Truview was used. This was in agreement with results of easier intubation that accounted for lower incidence of soft tissue trauma in their subjects.[8,9,10]

The trend in the changes of hemodynamic parameters in both the Truview group and Macintosh group followed the same direction, with MAPs and HRs higher during and after intubation compared to baseline. This can be partially explained by lesser force, as well as shorter intubation and laryngoscopy times with the Truview compared to the Macintosh.

This study has several limitations. The observers and intubators were not blinded to the device used and so

Table 3. Comparison of hemodynamic parameters between Macintosh and Truview groups.

	Macintosh	Truview	P value
Mean Arterial Pressure			
Baseline	92.7	86.9	0.176
During intubation	77.1	74.4	0.550
After intubation	100.2	86.9	0.007*
Heart Rate (mean)			
Baseline	81.1	78.55	0.599
During intubation	79.7	75	0.297
After intubation	95.6	88.3	0.127

Table 4. Pairwise comparison of mean arterial pressure for within group variability between Macintosh and Truview groups.

MAC/TRUVIEW	(I) MAP	(J) MAP	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval for Difference	
						Lower Bound	Upper Bound
MAC	1	2	15.625	3.445	0.001*	6.582	24.668
		3	-7.445	2.852	0.052	-14.931	.041
	2	1	-15.625	3.445	0.001*	-24.668	-6.582
		3	-23.070	3.918	0.000*	-33.354	-12.786
	3	1	7.445	2.852	0.052	-.041	14.931
		2	23.070	3.918	0.000*	12.786	33.354
TRUVIEW	1	2	12.500	4.091	0.020*	1.761	23.239
		3	-.005	4.511	1.000	-11.848	11.838
	2	1	-12.500	4.091	0.020*	-23.239	-1.761
		3	-12.505	1.999	0.000*	-17.753	-7.257
	3	1	.005	4.511	1.000	-11.838	11.848
		2	12.505	1.999	0.000*	7.257	17.753

Based on estimated marginal means where baseline mean arterial pressure is MAP, 2 - MAP during intubation, 3 - MAP after intubation. Bonferroni's test; significant at the 0.05 level.

Table 5. Pairwise comparisons of heart rate for within group variability.

MAC/TRUVIEW	(I) HR	(J) HR	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval for Difference	
						Lower Bound	Upper Bound
MAC	1	2	1.400	1.027	0.566	-1.296	4.096
		3	-14.450	2.793	0.000*	-21.783	-7.117
	2	1	-1.400	1.027	0.566	-4.096	1.296
		3	-15.850	2.670	0.000*	-22.858	-8.842
	3	1	14.450	2.793	0.000*	7.117	21.783
		2	15.850	2.670	0.000*	8.842	22.858
TRUVIEW	1	2	3.550	1.613	0.121	-.685	7.785
		3	-9.750	3.269	0.023*	-18.330	-1.170
	2	1	-3.550	1.613	0.121	-7.785	.685
		3	-13.300	2.961	0.001*	-21.074	-5.526
	3	1	9.750	3.269	0.023	1.170	18.330
		2	13.300	2.961	0.001*	5.526	21.074

Bonferroni's test; significant at the 0.05 level.

the potential for bias could not be eliminated. In conclusion, the Truview laryngoscope afforded better laryngoscopic view and optimal conditions for intubation in patients predicted to have difficult airways. The reduced hemodynamic stimulation was an added benefit.

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A double-blind randomized controlled trial on the effectiveness and safety of focused low frequency ultrasound waves in decreasing the abdominal circumference among healthy adults

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Abstract

Introduction Non-invasive focused low-frequency ultrasonic waves that reduce the circumference and volumes of areas with localized fat have become more popular. This study aimed to determine the effectiveness and safety of focused low-frequency ultrasonic waves in reducing localized abdominal fat deposits.

Methods This was a randomized, double-blind, placebo-controlled trial. Included in the study were Filipino adults with localized abdominal fat deposits. The primary outcome measure was mean change in abdominal circumference after 4 weeks of treatment, and secondary outcome measures were mean change in abdominal fat thickness, weight, serum lipid profile, as well as frequency of adverse events.

Results There was a significant reduction in the mean abdominal circumference and fat thickness among patients who received focused low-frequency ultrasonic waves compared to those in the placebo group. There were no significant differences in weight, total cholesterol, HDL, LDL, triglycerides, VLDL levels, and adverse events between the two groups.

Conclusion Focused low-frequency ultrasonic waves are effective in reducing abdominal circumference and fat thickness.

Key words: focused low-frequency ultrasonic waves, localized abdominal fats

Existing non-invasive and minimally-invasive technologies for improving the appearance of skin and subcutaneous fat appearance have gained popularity due to minimal downtime, relative safety and temporary cosmetic benefits. One of the US FDA-approved devices is an ultrasound waves-emitting device.[1] There is extensive discussion about the possible medical application of focused ultrasound in the minimally invasive treatment of a variety of disorders and diseases, one of which is lipolysis. This new technique is of great interest especially for those patients who do not intend to undergo invasive treatment for localized fat accumulation.[1]

Ultrasound waves induce both thermal and non-thermal physical effects in tissues. Non-thermal effects are said to be more important in treatment of soft tissue lesions. These non-thermal effects include cavitation which is the formation of tiny gas bubbles in the tissues as the result of ultrasound vibration.[2] This cavitation phenomenon occurs once the ultrasound sound waves propagate through the medium: the characteristic compression and rarefaction cause microscopic gas bubbles in the tissue fluid to contract and expand forming a "microexplosion".[3] Effects of cavitation that have been demonstrated in-vitro include stimulation of fibroblast repair, collagen synthesis, tissue regeneration, bone

healing and lipolysis in adipose tissues.[4] The lipolytic effect is said to be due to increasing secretion of plasma free fatty acid, epinephrine and norepinephrine concentration of adipose tissue.[5]

Low frequency ultrasound when applied directly to tissue delivers a physical force with a pressure of over 100 kg/cm^2 into the adipocytes and interstitial body fluid. These shockwaves and a micro jet of water emitted are capable of selectively damaging the membranes of fat cells causing lipolysis.[2] There have been numbers of studies showing that focused ultrasonic waves reduce circumference and volumes of areas with localized fat[2,6,7] and there was a significant relation between increase in lipid level and low-frequency ultrasound used. Most of these were open label and not randomized and blinded, making the results biased.[2,6,7] This study aimed to determine the efficacy and safety of low-frequency ultrasound waves in reducing abdominal fat circumference and volume compared to placebo.

The objectives of this study were to determine the difference of focused low-frequency focused ultrasound waves with placebo on the following: 1) abdominal circumference, 2) abdominal fat thickness, 3) weight, and 4) lipid profile.

Methods

This was a randomized, double-blind, placebo-controlled trial comparing focused low-frequency ultrasonic waves (FLFUW) with placebo in reducing abdominal fat in adults conducted at the Section of Dermatology of the Out-Patient Department of a tertiary hospital in Quezon City.

Healthy Filipino adults 20 to 50 years old, with localized abdominal fat deposits and with a body mass index (BMI) of 18.5 to 29.9 kg/m^2 were eligible to join the study. Those with any of the following were excluded: 1) pregnancy, 2) breastfeeding, 3) loose abdominal skin, 4) weak abdominal muscles, 5) scarring or active infection of the abdominal area, 6) history of keloid formation 7) use of medications known to induce photosensitivity (i.e., doxycycline, anti-malarials etc.), 8) metal implant and/or pacemaker, 9) tinnitus and migraine, 10) systemic illness (e.g., hypertension, diabetes mellitus, coagulation disorders, cancer), 11) lipid, hepatic and renal dysfunction, and 12) previous focused ultrasound wave or similar treatment or knowledge of how the procedure is performed.

The calculated sample size was 20, assuming a difference in means between treatment and control of 3.0 cm, a standard deviation (SD) of 1 cm, 80% power to detect a statistical significant difference, and level of significance at 0.05. To compensate for possible drop-outs or loss to follow-up of 20%, two additional patients per group or 12 patients per group, for a total of 24 subjects were recruited. Subjects were randomly assigned to the treatment group or placebo group using a computer-generated list of random numbers (www. random.org).

All patients underwent screening procedures including physical examination, CBC, liver function and serum lipid determination. Baseline demographic data, weight, height and BMI were recorded. Baseline photographs of the abdominal region were taken using a digital camera (Canon S90™) with the subjects standing at rotating angles, using constant lighting and focal distance. Abdominal circumference was measured at level of the umbilicus using a standard measuring tape. Abdominal fat thickness was measured at a standard area midway between the umbilicus and iliac crest using a caliper (recorded to the nearest millimeter).

Patients were then randomized into either FLFUW or placebo group. Patients in the FLFUW group received 20 minutes of focused low-frequency ultrasound waves of 44 kHz at power of 70% (~1.8 W/cm^2) on the abdomen per treatment session. Patients in the placebo group received 20 minutes massage using the transducer of the device but with no ultrasound waves delivered on the abdomen per treatment session. A 10% (~0.25 W/cm^2) power was used just to maintain a ringing sound. The apparatus used was LipoSlim™ which emits low frequency ultrasound waves 32 to 43 KHz through a 63 mm diameter transducer at a power of 50 to 100 watts/cm^2. A conductive gel was used (Medigel™) on all patients.

All patients underwent four treatment sessions at one week intervals and were followed up until a week after the last treatment. At the end of each treatment session, patients were photographed under the same controlled conditions and settings. Abdominal circumference, fat thickness and weight measurements were taken using the standard methods described. Each patient was instructed to record and report any adverse event that might arise during the course of the study. All measurements and photographs were taken by a person blinded to the treatment allocation. Serial serum lipid determinations were obtained 24 hours before the beginning of the first session, immediately after, after 96 hours, and on the fifth week after the first session.

The patients were instructed not to undergo other slimming procedures (mesotherapy, endermologie, radiofrequency, etc.), nor take any oral slimming medications, and to maintain baseline food intake and frequency of physical activities for the duration of study. They were also instructed to follow up four weeks after the last treatment for measurements and photographs.

The primary outcome was the mean change in abdominal circumference from baseline to week 4 between the treatment and control groups. The secondary outcomes were: 1) mean change in abdominal fat thickness, 2) weight from baseline to week 4, 3) mean change in serum lipids from baseline to just before the 1st treatment, right after, 96th hour after and 5th week after the 1st treatment, and 4) adverse events.

The T-test was used to compare the mean change in abdominal circumference, abdominal fat thickness and weight between groups. A paired T-test was used to compare the mean change in serial serum lipid levels within groups. Fisher's exact test was used to determine the difference in frequency of adverse effects between groups.

The study was approved by the Institutional Review Board.

Results

Twenty-four subjects were recruited to the study. As shown in Table 1, there was no difference in the mean age, sex distribution, BMI, weight, abdominal circumference and abdominal fat thickness of the FLFUW and control groups. Thus, the groups were comparable.

There was a decrease in the abdominal circumference of the patients in both groups four weeks into the study. The mean difference between week 4 and baseline measurements among the patients in the LFUW group was -5.67 cm compared with -1.38 cm in the control group. The difference between groups was significant up to week 4 but not at week 8. There was a decrease in the abdominal fat thickness of the patients in both groups, four weeks into the study. Specifically, the mean difference between week 4 and baseline measurements among the patients in the LFUW group was -5.92 mm compared with -1.17 mm in the control group. The difference between groups was significant ($P = 0.001$, Fisher's exact test). There was a minimal decrease in the mean weight of the patients as study progressed, regardless of the treatment that was given ($P > 0.05$, T-test). These results are shown in Table 2.

The mean change in total cholesterol of the patients in the FLFUW group seemed to increase slightly from 24 hours before the 1st session until 96 hours after the 1st session and decreased on the 5th week after the 1st session. Meanwhile, the mean change in total cholesterol of the patients in the placebo group appeared to decrease from 24 hours before the 1st session until 96 hours after the 1st session. This mean change in total cholesterol did not vary significantly within groups ($P > 0.05$, paired T-test). The mean change in HDL of the patients in the FLFUW group seemed to decrease from 24 hours before 1st session until the 5th week after the 1st session. Meanwhile, the mean change in HDL of the patients in the placebo group appeared to increase from 24 hours before the 1st session until the 5th week after the 1st session. Changes in both treatment arms were not statistically significant ($P > 0.05$, paired T-test). Rises and dips noted in the LDL, VLDL and triglycerides were not significant ($P > 0.05$, paired T-test). The changes in the lipid profile are shown in Table 3.

Adverse events in both the placebo and FLFUW groups occurred at the first week into the study. Half of the patients in the FLFUW group experienced adverse events: four had steatorrhea, while the other two experienced headache and pruritus in the area treated. One patient in the placebo group experienced transient headache. However, the difference in the occurrence of

Table 1. Demographic characteristics of patients in FLFUW and placebo groups.

Characteristics	FLFUW (N=12)	Placebo (N=12)	P-value
AGE (years) (mean ± SD)	35.75 ± 11.7	32.92 ± 7.9	0.48[a]
GENDER			
Male N(%)	4 (33.3)	5 (41.6)	1.00[b]
Female N(%)	8 (66.6)	7 (58.3)	
BMI in kg/m^2 (mean ± SD)	25.11 ± 2.6	24.12 ± 1.8	0.29[a]
Weight in kg (mean ± SD)	65.25 ± 10.5	63.54 ± 12.1	0.71[a]
Abdominal circumference in cm (mean ± SD)	92.42 ± 8.5	85.75 ± 8.8	0.07[a]
Caliper measurement in mm (mean ± SD)	32.75 ± 7.4	29 ± 5.2	0.18[a]

[a]Student T-test, [b]Fisher's exact test

Table 2. Mean change from baseline to week 4 into the study.

Primary outcome: Mean change in abdominal circumference		Baseline	Week1	Week 2	Week 3	Week 4	Week 8
FLFUW (N=12)	Mean change from baseline (cm) ± SD	---	-3.292 ± 2.1	-3.875± 3.2	5.083± 3.6	-5.67± 3.9	3.917± 5.0
Placebo (N=12)		---	-0.75± 0.9	-1.083± 1.8	-1.292± 1.9	-1.38± 1.3	-1.125± 1.5
	P value		0.0012	0.0169	0.0047	0.0017	0.0789
Secondary outcomes: Mean change in abdominal fat thickness							
FLFUW (N=12)	Mean change from baseline (mm) ± SD	---	-2.583± 1.9	-4.167 ± 2.2	-4.75 ± 3.2	-5.917± 4.2	-3.25± 2.5
Placebo (N=12)		---	-0.167± 0.3	-0.708 ± 0.9	-0.75± 1.1	-1.167 ± 1.1	-1.083 ± 1.4
	P value	---	0.0004	0.0001	0.0006	0.0010	0.0182
Mean change in weight							
FLFUW (N=12)	Mean change from baseline (kg) ± SD	---	-0.042 ± 0.1	-0.208 ± 0.7	-0.042 ± 0.6	-0.25± 0.9	-0.125± 0.7
Placebo (N=12)		---	0± 0.6	0.375± 1.1	0.125 ± 1.2	0.04± 1.1	-0.333 ± 0.8
	P value	---	0.8361	0.1413	0.6822	0.5177	0.5393

T-test

adverse events between the two groups was not significant (P = 0.07, Fisher's exact test).

Discussion

In this clinical study, all the patients treated with FLFUW had significant reduction in abdominal circumference and fat thickness measurements similar to the study of Micholvitz.[2] The absence of a significant reduction in weight is consistent with the study of Savoai.[6] The effect of FLFUW in decreasing abdominal circumference was not sustained beyond the 4 weeks of treatment. Thus, additional sessions until the desired reduction is achieved are recommended, and should be coupled with the proper diet and exercise.

Physical examination assessments and serial serum total cholesterol, HDL, LDL, VLDL, triglycerides levels throughout the study period showed no significant changes. The adverse events experienced in the FLFUW group appeared to be well tolerated and were not statistically different from the control group. All patients who experienced steatorrhea were in the FLFUW group, suggesting that fat was released from the treated area and possibly excreted through the bowel.

The authors conclude that FLFUW is an effective and a well-tolerated non-invasive technique for the reduction of abdominal circumference and fat thickness among healthy patients, and may be considered as an alternative to conventional liposuction, especially for those who do not wish to undergo invasive procedures. In a clinical setting, careful patient selection is imperative. They recommend taking the patient's complete history, BMI and baseline laboratory tests such as serum liver function and lipid profile prior to treatment to ensure that there are no co-morbidities and ensure the patient's safety. They recommend a clinical trial with larger sample size, a more controlled setting including standard diets and physical activities.

Table 3. Change in serial serum lipid (mg/dL) by treatment group.

			24 hrs before 1st session Mean ± SD	Right after 1st session Mean ± SD	96 hrs after 1st session Mean ± SD	5th week after 1st session Mean ± SD
Total Cholesterol	LFUW (N=12)	Mean ± SD	181.09 ± 24.9	188.36 ± 19.8	188 ± 19.6	180.73 ± 17.6
		Mean change	---	7.27 ± 15.2	0.81 ± 5.5	7.63 ± 4.6
	Placebo (N=12)	Mean ± SD	184.31 ± 11.9	180.92 ± 15.4	178.38 ± 18.2	184.31 ± 11.9
		Mean change	---	2.15 ± 5.2	8.53 ± 5.0	4.69 ± 2.1
	P value		---	0.2770	0.3167	0.5513
HDL	LFUW (N=12)	Mean ± SD	53.45 ± 5.8	52.18 ± 5.4	52.64 ± 4.9	52.27 ± 3.5
		Mean change	---	0.36 ± 2.8	1.18 ± 3.6	-0.9 ± 3.1
	Placebo (N=12)	Mean ± SD	56.31 ± 4.1	57.15 ± 6.5	58.46 ± 6.4	57.85 ± 5.6
		Mean change	---	0.61 ± 3.3	-1.76 ± 3.6	-0.69 ± 3.3
	P value		---	0.8462	0.0510	0.6540
LDL	LFUW (N=12)	Mean ± SD	109.82 ± 22.5	113.27 ± 18.0	111.46 ± 16.7	106.36 ± 18.6
		Mean change	---	5.09 ± 6.5	2.09 ± 19.9	6.9 ± 2.2
	Placebo (N=12)	Mean ± SD	112.46 ± 15.5	108.38 ± 13.4	102.92 ± 18.8	99.92 ± 21.4
		Mean change	---	3 ± 3.9	13.07 ± 19.9	8.46 ±10.9
	P value		---	0.3433	0.1921	0.1921
VLDL	LFUW (N=12)	Mean ± SD	19.18 ± 4.8	21.64 ± 5.7	23.64 ± 7.3	24.37 ± 7.9
		Mean change	---	-0.72 ± 9.4	-0.72 ± 9.4	-0.72 ± 9.4
	Placebo (N=12)	Mean ± SD	20 ± 9.5	17.38 ± 8.5	18.23 ± 9.7	18.69 ± 8.6
		Mean change	---	-0.46 ± 3.5	-0.46 ± 3.5	-0.46 ± 3.5
	P value		---	0.9256	-0.9256	0.9256
Triglycerides	LFUW (N=12)	Mean ± SD	99.55 ± 30.6	107.36 ± 28.3	115.64 ± 36.6	118.18 ± 39.5
		Mean change	---	-2.54 ± 46.6	-17.09 ± 41.6	-10.81 ± 54.8
	Placebo (N=12)	Mean ± SD	98.38 ± 44.9	83.08 ± 33.9	90 ± 33.0	97.15 ± 42.1
		Mean change	---	-7.15 ± 25.3	1.84 ± 41.6	-14.07 ± 25.5
	P value		---	0.7616	0.2215	0.8499

Paired T-test

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Re-evaluating the efficacy and safety of citicoline in acute ischemic stroke: a meta-analysis

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Abstract

Introduction This meta-analysis aimed to re-evaluate the evidence obtained from randomized controlled trials on citicoline in the treatment of acute ischemic stroke by determining the efficacy of citicoline in terms of post-treatment functionality and its safety.

Methods Studies were included in the meta-analysis after a systematic, computerized search if they met the criteria. The primary outcome was clinical improvement measured by the Barthel Index. An intention-to-treat analysis was done. The data were analyzed using the Review Manager 5 and odds ratios were determined.

Results The five trials included had 4,121 patients, with a mean age of 69.7 years, admitted for an acute ischemic stroke or infarct within 24 hours to 14 days of the onset of neurologic symptoms. The citicoline group consisted of 2,194 patients, while 1,927 patients were given placebo. The mean baseline NIHSS score was 13.7. There were no significant differences between treatment and control groups in terms of efficacy and safety.

Conclusion Citicoline is safe but not efficacious in the treatment of acute ischemic stroke.

Key words: citicoline, acute ischemic stroke

Stroke continues to be one of the most deadly and debilitating diseases. It accounts for 10% of deaths worldwide – 5.7 million in 2005.[1] It ranked second in the "Ten Leading Causes of Mortality", next to diseases of the heart, in the Philippines in 2006.[2] It is a leading cause of long term disability in both developed and developing countries. According to the World Health, Organization the prevalence of stroke was 14 per 1,000 people in the Philippines in 2005.[1] Three community-based studies conducted locally[3-5] showed the prevalence to be between 0.5 – 1.9%. Due to the possibility of serious disability, stroke remains to be a medical emergency, and a number of clinical trials have been conducted to discover effective treatment.[6]

Neuroprotection, coupled with recanalization via thrombolysis with recombinant tissue plasminogen activator (rTPA), are the cornerstones of treatment of acute ischemic stroke. Adequate blood pressure control and oxygenation, normoglycemia, proper nutrition, hypothermia, and coupled with various pharmacologic agents have been used to salvage the ischemic penumbra. Of the many drugs available, citicoline is one of the most extensively studied, especially for ischemic strokes. It is the exogenous form of cytidine-5-diphosphatidylcholine, an essential precursor of phosphatidylcholine, a major structural component of cell membranes that becomes degraded to highly toxic substances, such as free fatty acids and free radicals, during cerebral ischemia.[7] It acts at several levels of the ischemic cascade, and has been shown to have reparative effects, reversing increased free fatty acid formation and loss of phosphatidylcholine.[6,8-9]

Although individual trials on humans have been inconclusive, a meta-analysis of 10 trials by Saver in 2008 suggested that patients who received citicoline had substantially reduced frequencies of death and

disability.[10] Results from this review were encouraging, and suggested a moderate but real benefit of the drug in acute and subacute stroke.[10]

In 2006, International Citicoline Trial on Acute Stroke (ICTUS), the most recent, and to date, the largest, clinical trial on the efficacy and safety of citicoline, enrolled 2,298 patients from different centers in Europe. Results of the ICTUS trial have shown that global recovery was similar for both treatment and control groups, as well as safety variables and rate of adverse events.[6] The study concluded that under the circumstances of the trial, citicoline is not efficacious in the treatment of moderate to severe stroke.[6] A meta-analysis, updating that of Saver was done by the ICTUS Trial Investigators, incorporating the results of their present study. They defined success as a Modified Rankin Score (mRS) of 0 – 2 and found that citicoline had no significant effect in the treatment of acute ischemic stroke.[6]

Both these recent meta-analyses included a subset of patients where the primary outcome measure was determined by neuroimaging findings. In this light, the investigators thought of re-evaluating the efficacy and safety of citicoline based clinical improvement. The objective of this study was to re-evaluate the evidence obtained from randomized controlled trials on the efficacy and safety of citicoline in acute ischemic stroke. The specific objectives were to determine the efficacy of citicoline in terms of post-treatment functionality, as measured by the Barthel Index, and to confirm the safety of the drug.

Methods

A systematic online search was conducted through PubMed, MEDLINE with full text and CINAHL with full text (via EBSCOHost), MDConsult, and the Cochrane Library using the terms (*citicoline* OR *CDP-choline)* AND (*stroke* OR *cerebral infarct*). The search was limited to studies in humans, written in English, from January 1, 1960 to September 30, 2012. A free text search was also done via ResearchGate, Yahoo, and Google, using various permutations of the search terms: "citicoline" or "CDP-choline", with "stroke" or "cerebral infarct". A search of the references of the identified articles was also done. When the results of a study were reported in more than one publication, the latest and most comprehensive data were used.

Only randomized controlled trials comparing the efficacy and safety of citicoline with placebo in the treatment of acute to subacute, moderate to severe, ischemic stroke were included. No age and gender limitations were set. The intervention was citicoline, administered orally or intravenously at any dose, frequency and duration. The primary outcome was clinical improvement and functionality measured by the Barthel Index. Secondary outcomes were improvement in other scale scores (Global Improvement Rating, Global Usefulness Rating, National Institute for Health Stroke Scale, Modified Rankin Score, and Barthel Index), cognitive function, mortality, full recovery, treatment differences between groups, and length of hospital stay. Only studies with an intention-to-treat analysis were included.

The articles retrieved were screened for appropriateness to the investigators' research question. The full texts of the articles that passed the screening were appraised by at least two investigators. The methodological quality of the eligible randomized controlled trials were assessed using the Jadad Scoring System, with the lowest score being 0, and the highest score, 5.[11] Differences in appraisal were resolved by a third reviewer. The following data were extracted from the included studies: year of the study, number of participants, demographics, inclusion and exclusion criteria, citicoline dose and frequency, duration, assessment tools, treatment outcomes, and adverse events.

Review Manager 5 (RevMan 5), provided by the Cochrane Collaboration, was used to organize and analyze the data. The odds ratio (OR) and 95% confidence interval was computed for each of the primary outcomes. Chi-square and I^2 values were determined to assess heterogeneity; a P value of <0.05 was considered significant. The fixed effects model was used for studies that were homogeneous, and the random effects model, for studies with significant heterogeneity. The authors regarded an I^2 of 0-40% as not important, 41%-60% as moderate heterogeneity, 61%-75% as substantial heterogeneity, and more than 75% as high.[12] Publication bias was estimated visually by funnel plots.

Results

The authors identified 77 articles through PubMed (18), MEDLINE with full text and CINAHL with full text via EBSCOHOST (12), Cochrane Library (3), and MDConsult (12). As of September 2012, no new clinical trials on the efficacy of citicoline in acute ischemic stroke have been published. Six randomized controlled trials were identified for inclusion (Tazaki[13], Clark[9,14,15] Davalos[6] and Warach[16]). The rest were excluded because they were animal studies, commentaries, review articles, studies using the drug for another disease condition, or duplicate reports. The study by Warach was eventually

excluded because it assessed improvement in terms of reduction of the volume of the infarct based on CT scan.

Five trials were included in the study and their characteristics are summarized in Table 1. The five trials had a total of 4,121 patients from 294 stroke centers admitted for an acute ischemic stroke or infarct within 24 hours to 14 days of the onset of neurologic symptoms; 2,194 were treated with citicoline, while 1,927 were given placebo. The mean age was 69.7 years, with a male to female ratio of 1:1. The mean baseline NIHSS score for four trials[6, 9, 14,15] was 13.7. The citicoline groups received 500 - 2000 mg per day, orally or intravenously, as single or two divided doses, within 24 hours – 14 days of onset of symptoms, for 14 days to 6 weeks. Primary outcomes of post-treatment functionality were measured at 14 days to 6 weeks. Tazaki[13] used the Japan Coma Scale (JCS), Global Improvement Scale (GIS) and Global Usefulness Rating (GUR); Clark[9, 14,15] used the Barthel index at 12 weeks; and Davalos[6] used several scales (NIHSS, modified Rankin scale and Barthel Index) at 12 weeks. Secondary outcomes are listed in Table 2. More than 20% of subjects dropped out for one of the following reasons: death, discharge from admission, lost to follow-up, transfer to another hospital, adverse effects (attributable to the drug or not), switching to another treatment, and poor drug compliance. The methodological quality of the studies was good, with all of them obtaining scores of at least 4 on the Jadad Scale.[12] Four studies failed to include a description of the randomization.

Table 1. Characteristics of included studies.

	Tazaki 1988 (Japan)	Clark 1997 (USA)	Clark 1999 (USA)	Clark 2001 (USA)	Davalos 2012 (Europe)
Type of Study	Double blind placebo controlled trial trial	Randomized double-blind vehicle-controlled efficacy trial	Randomized double blind placebo-controlled efficacy trial	Randomized double blind placebo-controlled efficacy trial	Randomized double blind sequential placebo controlled trial
Duration of Study	November 1982-February 1985	June 1994 - August 1995	June 1996 - July 1997	August 1997 - November 1998	November 2006 - October 2011
No. of Patients	272	259	394	898	2298
No. of Centers	63	21	33	118	59
Males	183	121	185	467	1156
Females	89	138	209	432	1142
Age Range or Mean Age, years	29-90	67.8	70.5	67.8	72.8
Citicoline Dose	1000mg IV daily	500mg, 1000mg, 2000mg oral daily	500mg oral daily	2000mg oral daily	2000 mg IV per day for 3 days then 1000 mg per day
Intervention Dosing	Once daily	Once daily	Once to twice daily	500 mg 2 tablets twice daily	1000 mg IV every 12 hours, then 500 mg tablet twice daily
Mean Baseline NIHSS	-	12.85	13	14.2	15
Jadad Score	4	4	4	4	5

Table 2. Primary and secondary outcomes.

	Tazaki 1988 (Japan)	Clark 1997 (USA)	Clark 1999 (USA)	Clark 2001 (USA)	Davalos 2012 (Europe)
Primary Outcome	Improvement baseline (Global Improvement Scale; Overall Safety rating; Global usefulness rating)	Functional outcome (Barthel index at 12 weeks)	Functional outcome (Barthel Index at 12 weeks)	Improvement from baseline (NIHSS by more than or equal to 7 points by the end of week 12	Global recovery (NIHSS, mRs, Barthel index)
		Secondary outcomes: 1) Barthel index at other weeks 2) percentage of patients with full recovery 3) treatment differences (Modified Rankin Scale) 4) treatment differences on neurological, behavioral, and cognitive function (NIHSS & MMSE) 5) mortality 6) full recovery, NIHSS > or equal to 1 7) length of hospital stay 8) relative rate of improvement (Barthel Index, nRS & NIHSS) between groups	Secondary outcomes: 1) Barthel index at other weeks 2) percentage of patients with full recovery 3) treatment differences (Modified Rankin Scale) 4) treatment differences on neurological, behavioral, and cognitive function, (NIHSS & MMSE) 5) mortality 6) full recovery, NIHSS > or equal to 1 7) length of hospital stay 8) relative improvement (Barthel Index, nRS & NIHSS) between groups	Secondary outcomes: 1) proportion of patients who returned to prestroke Barthel index score at 12 weeks 2) proportion of patients who improved (clinician's global impressions) scale 3) proportion of patients with a greater than or equal to 2-point improvement (CGI severity scale) 4) mortality 5) treatment differences at 12 weeks (overall response analysis based on NIHSS improvement greater than or equal to 7, Barthel index return to prestroke values, CGI improvement of 1 -2, and CGI severity improvement of greater than or equal to 2 6) assessment of treatment differences in the volume of ischemic lesions via conventional T2 weighted MRI	Secondary outcomes: 1) rate of favorable response to single scales 2) between groups comparison of distribution of mRs scores 3) absolute difference (NIHSS) between baseline and 3 months

For purposes of this meta-analysis, the post-treatment improvement functionality was determined by the Barthel Index score, 85 – 100, for the studies of Clark[9, 14,15] and Davalos[6], and the GIR score, for the study of Tazaki[13]. As shown in Figure 1, the results were heterogeneous, requiring the use of the random effects model for analysis. The over-all odds ratio was 1.35, which was not significant. After excluding the study by Tazaki, the results became homogeneous; the odds ratio was 1.05 and still not significant.

A safety analysis including all trials showed no significant difference in the mortality between treatment and placebo groups as shown in Figure 2. There was no difference between treatment and control in the other adverse events (cardiac/cardiovascular disorders; gastrointestinal events, such as constipation, nausea and vomiting; conditions related to the central nervous system such as hemorrhagic stroke, headache, and dizziness; respiratory diseases, such as pneumonia; and urinary tract infection; falls and other injuries, and skin rash).

Discussion

Various clinical and experimental trials done over the past few years suggesting the efficacy of citicoline in protecting the ischemic penumbra during an acute stroke has made the drug a mainstay in the treatment of the disease. A meta-analysis by Saver[11] evaluating the efficacy of citicoline in different types of stroke showed the drug to have a highly significant treatment effect when the analysis was confined to the four largest trials[11]. However, a meta-analysis done later by Davalos as part of the ICTUS Study showed that on top of best treatment, citicoline did not show any further improvement; however, the effect of the drug remained significant.[6] This meta-analysis shows that there is no significant advantage in giving citicoline for acute moderate to severe stroke in terms of efficacy. In agreement with the authors of the ICTUS Study, the heterogeneity coming from the older studies suggested that the beneficial effect of citicoline over time came with the improvement of the standard of care of acute ischemic stroke.[6]

This meta-analysis confirmed that citicoline is safe to give in patients with moderate to severe acute ischemic stroke. The adverse events observed in the trials included in this analysis were not due to the administration of the drug to the treatment groups.

There are limitations and potential biases in this study. First, this meta-analysis to included studies on

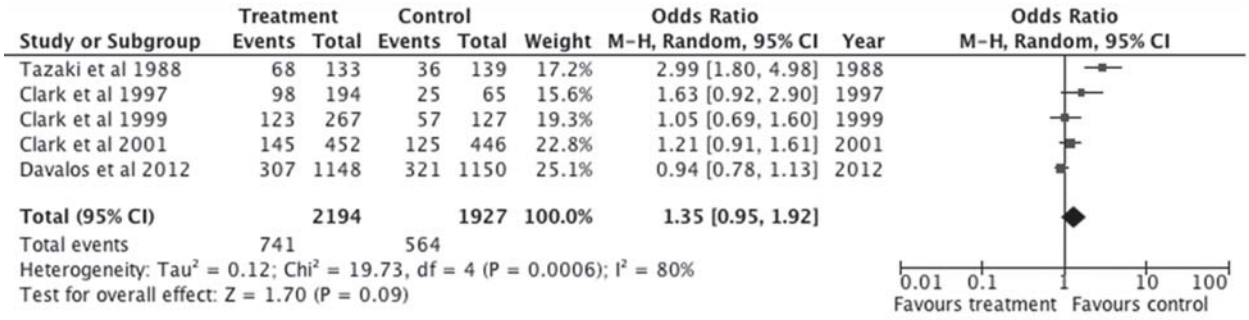

Figure 1. Over-all functionality after treatment with citicoline at 12 weeks (Barthel Index).

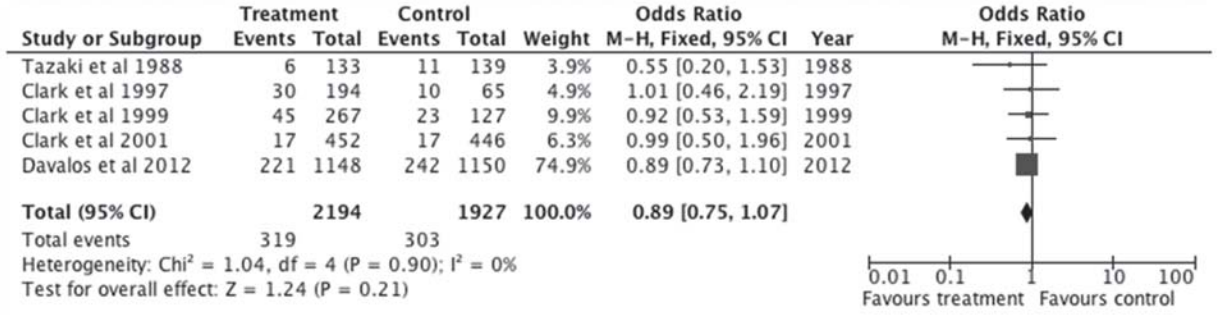

Figure 2. Safety analysis of citicoline for acute ischemic stroke.

patients confirmed to have ischemic strokes but Tazaki[13] had patients with "undetermined" strokes. This group could not be removed from the actual pool used the analysis. Second, the study was on patients with moderate to severe stroke; the possible benefit of citicoline to patients with mild stroke was not considered. Third, the Barthel Index of the patients in study of Davalos, (95-100), was used as the measure of the primary outcome, with the assumption that this would be comparable with the other trials. Because of this, the patients whose Barthel Index was below 95 but above 85 were not considered in the analysis of the primary outcome. Fourth, the authors did not assess the events concerning the secondary outcomes of the trials. Fifth, not all the studies on citicoline may have been retrieved despite the extensive effort. Publication and location bias may have occurred. And lastly, the systematic search for articles was limited to those written in or translated to the English language.

In conclusion, citicoline is safe, but not efficacious, in the treatment of moderate to severe acute ischemic stroke. The authors recommend that future studies on the efficacy of the drug, under variable clinical conditions, and different populations, be made to determine its possible benefits and to verify effects seen in other trials.

Declaration of conflict of interest

The authors have no known conflicts of interest that may influence their judgment in making this meta-analysis. This study did not receive any funding nor technical assistance from any company or agency.

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Quality of life of Filipino elderly with dementia (QoL-FD) assessment tool: Its development, validation and standardization

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Abstract

Introduction Life value should also be considered in an elderly person with dementia, aside from the medical attention. An assessment of the quality of life will provide a substantial impact in the clinical practice, disease severity, and evaluation of treatment outcomes provided for this condition. In the Philippines, the use of a self-constructed instrument to assess the quality of life specifically among this group is very limited; hence developing a culturally sensitive quality of life measure was the thrust of this study.

Methods The research utilized test construction methodology to develop the Quality of Life of Filipino Elderly with Dementia (QoL-FD) tool. In the item generation stage, a multi-source approach was done utilizing in-depth interviews with elderly with dementia, caregivers, a neurologist and other health allied practitioners specializing in dementia. The draft underwent face validation by the experts and was administered to a sample of 5 patients in a private hospital's memory clinic. The final form of Quality of Life of Filipino Elderly with Dementia (QoL-FD) tool was pretested in a sample of 211 community-dwelling elderly in a city in the metropolitan area.

Results From the pool of samples, 20 elderly were diagnosed to have mild to moderate level of dementia. During the preliminary testing, the items generated convergent validity with WHOQOL BREF. To test the internal reliability, a Spearman Brown formula and Cronbach's alpha coefficient were computed and showed that it was a valid and reliable instrument.

Conclusion In the final form, the tool had a validity value with Pearson r of 0.90, split half reliability value using Spearman Brown formula of 0.92 and Cronbach's alpha of 0.90. Thus, the QoL-FD is a psychometrically sound instrument for measuring quality of life.

Key words: Dementia, Alzheimer, Quality of Life

Quality of life (QoL) is a multidimensional concept and has been broadly defined by the World Health Organization (1995) as an individual's perception of his or her position in life in the context of his or her culture and value system. It is also the integration of cognitive functioning, activities of daily living, social interactions, and psychological well-being.[1] Health greatly affects one's component of achieving quality of life. In chronic neurodegenerative diseases like dementia which is prevalent in the elderly, a range of cognitive and behavioral symptoms and functional impairment occurs that makes the person gradually dependent on others for activities of daily living. It is always presumed that this lack of independence is always associated with poor quality of life. As a demented patient, the presence of cognitive decline and functional impairment make him vulnerable to a poor quality of life.

In dementia research and practice, there has been a long-unchallenged assumption that people with dementia cannot give a reliable account of their own quality of life.

This often leads to an assumption that people with dementia cannot achieve a positive QoL in the presence of physical disease. A study done abroad[2] showed little or no association between QoL and severity of cognitive impairment for people with mild to moderate-stage dementia. Just because an individual's cognition worsens, it cannot be assumed that this inevitably leads to worsening of QoL. The importance of developing QoL measuring instruments for people with dementia is as important as measuring the disease's severity, progression, symptom response, cognition, behavioral disturbances, and activities of daily living when assessing the impact of disease and intervention in dementia.[3] At present, Lawton's model of QoL is used as a framework of QoL tests that are foreign-made[4], but its utility may be limited in Philippine culture. Furthermore, the existing QoL instruments are mostly limited to health status assessment and do not deal with the impact of dementia among elderly. The thrust of this study is to develop a QoL instrument for the Filipino elderly with dementia where item-domains are generated from their own life experiences, values, perceptions and expectation of a quality life.

This endeavor will promote holistic quality of care for the demented elderly population since the primary goal of health care is geared towards increasing life expectancy and improving quality of life. Neurological illness may result in a limited means of expression, fatigue and cognitive decline that makes the QoL assessment and judgment of treatment efficacy difficult. Thus, with a tool that will measure the quality of life among Filipino elderly with dementia, appropriate intervention can be generated to improve the well-being of the elderly.

Methods

A test development framework design was utilized. It involved item construction, development of final form, and establishment of its psychometric properties by different reliability and validity procedures. The final phase involved standardization and establishment of norms.

Purposive sampling was utilized in this study. The participants came from a tertiary hospital's memory center and community dwellers in a city in the metropolitan area. The inclusion criteria were as follows: 1) age 60 years or older; 2) diagnosed to have probable dementia by the NINCDS-ADRDA criteria (Mini Mental State Examination score of 12 or above, signifying a mild to moderate stage); 3) MOCA scores below 26, signifying an impairment; 4) Clinical Dementia Rating (CDR) of 0.5 to 1, indicating mild stage; 5) availability of reliable collateral informant/s, preferably close family member/s who live/s with the patient or who is/are familiar with the patient's cognitive state.

Neuropsychological tests served as basis for selecting participants with dementia. The tests were also used in the psychometric testing during the validation of the Quality of Life in Filipino Elderly with Dementia (QoL-FD) assessment tool. The Montreal Cognitive Assessment (MOCA)[5] assessed different cognitive domains such as orientation, attention, memory, verbal fluency, naming, visuospatial /executive function, language, abstraction, and delayed recall. It has a cut-off score of 26. The MOCA detects 90% of mild cognitive impairment and its specificity is 100%. The Geriatric Depression Scale (GDS)[6] is probably the most common version currently used to measure depression in older adults with a cut-off score of 6/7. The GDS was found to have 92% sensitivity and 89% specificity when evaluated against diagnostic criteria. The Clinical Dementia Rating (CDR) is a global measure of dementia[7] used for detecting and staging the severity of dementia with a 5-point scale in which CDR-0 connotes no cognitive impairment and the remaining four points are for various stages of dementia. CDR detection of dementia among healthy elderly and questionable dementia are 86% and 80% sensitive, respectively, and 100% specific for both settings. The *WHOQOL-BREF* is a 26-item short form version of the WHOQOL-100[8]. It is a generic assessment of QoL across four domains: physical health, psychological, social relationships, and environment.[9]

IBM Statistical Product and Service Solutions (SPSS Statistics) version 17 was used to analyze data. Frequency and descriptive statistics (mean and standard deviation) were used. Internal consistencies of the scales used in the study were subjected to reliability and validity analysis using Pearson product moment correlation and Spearman Brown formula. Contrasted group method and item analysis were also employed to test the psychometric properties of the developed tool. Percentile scores were obtained for the conversion of the norms.

Results

During the preliminary phase of the test development, 211 elderly were screened. Of these, 20 were considered with dementia and met the inclusion criteria. Their Clinical Dementia Rating was within CDR = 0.5 (very mild dementia). For the final form, 360 elderly were screened and underwent a neuropsychological assessment. One hundred one met the inclusion criteria. Table 1 summarizes the demographic profile and characteristics of the participants.

Table 1. Demographics of the participants in the preliminary and final phases.

Characteristic	Preliminary Form (N=20)		Final Form (N= 101)	
	Frequency	Percentage	Frequency	Percentage
Gender				
Male	6	30	30	29.7
Female	14	70	71	70.3
Age				
60-65	6	30	27	26.7
66-70	6	30	25	24.8
71-75	2	10	26	25.7
76-80	4	20	12	11.9
81-85	2	10	11	10.9
Educational Attainment				
Elementary level	4	20	17	16.8
Elementary graduate	5	25	18	17.8
High school level	2	10	7	6.9
High school graduate	7	35	12	11.9
College level	2	10	13	12.9
College graduate	0	0	33	32.7
Vocational course	0	0	1	1
Level of Dementia				
CDR = 0.5	17	85	96	95.05
CDR = 1.0	2	10	4	3.96
CDR = 2	1	5	1	1
CDR = 3	0	0	0	0

Phase I: Conceptualization and Item Generation of QoL-FD

The domain compositions of QoL-FD tool were generated from experts in the discipline. The paradigm of WHOQOL and Lawton's Theory and in-depth interviews served as basis in the formulation of the items. Interviews were conducted with elderly with dementia, caregivers and a physician to identify their perceptions about quality of life and knowledge on dementia. From the five elderly respondents, experiences in their lives were expounded and variations from physical, psychological, social, and spiritual and memory constructs were generated from them. The caregivers, on the other hand, validated the actual changes that the elderly with dementia experienced they observed while taking care of their patients. The physician expert provided comprehensive information on the disease progression and validated the changes in cognition, memory, activities of daily living, and emotional and behavioral responses of elderly with dementia. The quantitative responses provided by the initial sample were organized into domains. These domains had ten items on each subscale. Verbatim quantitative responses were graded using a 4-point Likert scale as follows: 1 = poor, 2 = fair, 3 = good and 4 = excellent. A pool of 60 items generated across six domains (physical health, psychological, social, environmental, spiritual, memory) was then subjected to face and content validity by the following resource persons: neurologist, psychologist, nurse and Filipino professors.

Phase II: Preliminary Phase

The first draft of the QoL-FD tool which was pilot tested to establish its psychometric properties showed 20 (16.52%) elderly meeting the criteria out of 211 who were screened. Table 2 shows the convergent evidence of validity. The WHOQOL-BREF test adapted by a local investigator[10] was used to assess the quality of life among ambulatory and community dweller elderly. The Pearson correlation (0.96) showed a very high correlation between WHOQOL-BREF and the QoL-FD tool. Furthermore, a split half reliability type was

computed. Its reliability using Spearman Brown formula generated very high correlation (0.98) and the internal consistency of the items as indicated by the Cronbach's alpha (0.98) confirmed that the domains of the test and the items measured the same component. The validity and reliability of the QoL-FD preliminary form served as a basis for the Quality of Life of Filipino Elderly with Dementia (QoL-FD) tool.

Phase III: Final Phase

This phase involved the administration of the final form of the QoL FD tool. After item analysis, using percentage endorsement, the 60 items in the initial test were reduced to 33 questions. Table 3 shows the overall evaluation of each item. Percent endorsement statistics for each item indicate the proportion of the respondents who chose specific answers in the items.

To strengthen its psychometric property, the final form of QoL-FD was administered to 101 participants in the final phase. Table 4 shows very high correlation scores convergent validity scores using Pearson correlation. To test the internal consistency of the instrument, the degree of reliability was measured using the Spearman brown formula and showed a very high reliability. The internal consistency of the items as indicated by the Cronbach's coefficient alpha was also high enough to substantiate the reliability of the final form. Thus, the QoL-FD was shown to be a valid and reliable instrument in measuring quality of life among elderly with dementia with very stable psychometric properties.

The QoL-FD final form was also subjected to reliability tests. Using split half reliability, the items were divided into two parts and were analyzed using Pearson r values and Spearman Brown formula. The physical, social, environment and memory Pearson r value and Spearman brown values ranged from 0.50 - 0.70, while high correlation values (0.71-0.80) were

Table 3. Percentage distribution of the items for the domains of final form.

Domains	N	% Item	Number
Physical Health	6	18.18%	1, 2, 5, 6, 9, 10
Psychological	7	21.21%	2, 3, 4, 6, 7, 8, 10
Social Relationship	2	6.06%	5, 9
Environmental	6	18.18%	1,4, 5,7, 9, 10
Spiritual	5	15.62%	4,6,7,9,10
Memory	7	21.21%	2,3,6,7,8,9,10
Total	33	100%	

Table 2. Convergent evidence of validity and split half reliability values in the preliminary form.

	Statistical Treatment	Coefficient values	Interpretation
Validity measures	Pearson correlation	0.96	Very high correlation
Split half reliability measures	Spearman Brown formula (equal length)	0.98	Very high correlation
	Cronbach's alpha coefficient	0.98	Very high correlation

Note: **. Correlation is significant at the 0.01 level (2-tailed). All the alpha values p< 0.05

Table 4. Convergent evidence of validity and split half reliability values in the final form.

	Statistical Treatment	Coefficient values	Interpretation
Validity measures	Pearson correlation	0.90	Very high correlation
Split half reliability measures	Spearman Brown formula (equal length)	0.92	High correlation
	Cronbach's alpha coefficient	0.90	High correlation

Note: **. Correlation is significant at the 0.01 level (2-tailed). All the alpha values p< 0.05

obtained for the psychological and spiritual domains. The QoL-FD final form domains show higher consistency in their responses to the items of the QoL-FD, thus the domains comprising the QoL-FD measured are reliable.

A test is standardized when it has clearly specified procedures for administration and scoring including normative data. The statistical treatment of the final form served as the basis for constructing the norms of the QoL-FD. Percentile scores were computed from the raw scores generated from the responses of the participants to the final form of QoL-FD. Furthermore, a computation of the z-scores and t-scores was also utilized to provide more comprehensive values generated from the QoL-FD. Table 5 describes the sample norm equivalent.

Table 5. General description of raw scores and percentile rank of QoL-FD.

Raw Scores	T scores	Verbal Equivalent
85-134	51-67	Excellent quality of life
60-84	42-50	Good quality of life
34-59	33-41	Fair quality of life
33-below	1-32	Poor quality of life

The scores obtained from the QoL-FD served as the basis for the percentile ranking. The verbal descriptions of the norms were: excellent, good, fair and poor, which were also the categorical choices in the items in the QoL-FD tool.

Discussion

Quality of life had been explored in foreign and local literature and is an issue for disorders like Parkinson's disease, dementia, Alzheimer's disease and epilepsy.[11] There have been studies conducted on the quality of life in different courses of health care.[12, 13] They showed that measuring the efficacy of any treatment involves understanding the mechanism of the quality of life of these patients. This holds true for Alzheimer's disease - the most common neurological disease in the elderly. Based on the estimated prevalence in America, at age 65, elderly are susceptible to have AD and it doubles every five years.[14]

In the recent trends in the development of QoL measures, utility-based, rather than psychometric measures of quality of life, are necessary before any cost-effectiveness analyses can be performed. This utility-based measurement of quality of life has assumed greater importance in AD research.[15] To date, no QoL instrument used in clinical trials of anti-dementia drugs appears to be satisfactory[16] not because of the ineffectiveness of QoL in clinical trial outcomes, but rather, the tool itself has limited psychometric properties. Currently, though other self-measure tests for QoL such as the BASQID[17] and QOLAS[18], which are self-rated instruments and are good predictors of quality of life measures in dementia outcome, their utility had not been tested in our current population and literature suggests that a tailored fit instrument that is culturally sensitive in assessing quality of life is warranted.[9] At present, there is no gold standard for assessment of quality of life among Filipinos. The available QoL instruments are very broad and not culturally-based to provide adequate measures of one's own perception of the quality of life of the elderly population. The need for the development of a QoL tool for a specific culture continues to intensify as the outcome of intervention and improvement of quality of life become significant in dementia. This tool may also be considered as an adjunct tool for neuropsychological assessment by the health practitioners.

A limitation of the current study is the sample size which was insufficient to provide a general norm. The utility of QoL-FD in various forms of dementia to strengthen its applicability in the evaluation of intervention outcomes can also be expanded to enhance the instrument's content and psychometric variability. Future larger scale studies utilizing the demographic data and treatment outcomes of demented elderly in relation to their quality of life measured by the QoL-FD are warranted. Moreover, further studies are needed to determine the most important predictor of quality of life among the six domains in the QoL-FD.

Based on the findings, we concluded that Quality of life of Filipino Elderly with Dementia (QoL-FD) tool is a valid and reliable instrument in measuring the perception and experiences of the elderly's quality of life in the course of their dementia.

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A comparison between local wound exploration and focused assessment with sonography for trauma in the diagnosis of injury secondary to abdominal gunshots and stab wounds

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Abstract

Introduction The objective of this study was to compare the accuracy of Focused Assessment with Sonography for Trauma (FAST) with Local Wound Exploration (LWE) in detecting intra-abdominal injuries for patients with abdominal gunshot and stab wounds by calculating the sensitivity, specificity, predictive values and likelihood ratios of each diagnostic modality.

Methods This is a cross-sectional study conducted from June 2009 to June 2011 at a tertiary government level II trauma center in Manila. Included in the study were the medical records of all patients treated for abdominal gunshot and/or stab wounds. The following data were obtained from the records: demographic profile; mechanism of injury, whether gunshot or stab; location of injury, whether anterior, posterior abdomen (back); diagnostic procedures and results, whether FAST, local wound exploration, or both; management, whether surgical or conservative; and intraoperative findings, including organ/s injured, if any. For the gold standard, the subjects were categorized as positive or negative injury based on the laparotomy findings or, in the absence of surgical intervention, recovery without sequelae. The results of FAST and LWE were compared to the results of the gold standard by calculating the sensitivity, specificity, positive predictive value, negative predictive value and likelihood ratio with 95% confidence interval, for each modality.

Results The study included 95 subjects with a mean age of 31 years. Sixty eight (68) patients (71.6%) underwent FAST while 62 (65.3%) underwent LWE. There were 35 patients (36.8%) who underwent both the FAST and LWE. A total of 78 patients had anterior abdominal stab and gunshot wounds. FAST was more specific (97%) than sensitive (36.5%); LWE, however, was more sensitive (95%) than specific (50%). The positive predictive value of FAST was 100% while that of LWE was 77.6%. FAST had a low negative predictive value at 32.7% while LWE had a high negative predictive value of 84.6%. FAST had a higher positive likelihood ratio than that of negative likelihood ratio (12 versus 0.635). LWE, on the other hand, had a lower positive likelihood ratio of 1.9 but a high negative likelihood ratio of 0.1. The confidence intervals of the accuracy estimates were moderately precise.

Conclusion This study showed that LWE is an accurate diagnostic procedure in detecting traumatic injuries, while FAST is accurate in ruling out significant injury in patients with abdominal stab and gunshot wounds. For patients with suspected intra-abdominal injury, LWE should be done first as a screening test followed by FAST as a confirmatory test.

Key words: Abdominal injuries; wounds, penetrating; ultrasonography

The management of abdominal gunshot and stab wounds has continued to evolve over the years, from mandatory celiotomy to serial physical examination, local wound exploration and the use of diagnostic imaging techniques. The indications for surgery have drastically decreased over the years, with the advent of new non-invasive modalities like computerized tomography scan (CT scan) and ultrasonography. Researchers continue to evaluate various protocols but despite the advances in technology, the optimum method to determine the need for laparotomy has yet to be definitively established. The aim has always been to reduce the number of unnecessary operations without increasing the number of missed injuries, as well as to reduce the length of hospital stay and healthcare costs.

Before the era of diagnostic imaging, most of these patients underwent mandatory celiotomy. In the mid-seventies, studies[1,2,3] started to show that the combination of local exploration and peritoneal lavage in lower chest and abdominal stab wounds increased diagnostic accuracy, eliminated unnecessary hospitalization and reduced the number of negative laparotomies. Seventy percent of patients were spared an operative procedure, and the incidence of negative laparotomy decreased to less than 5%.

The advent of non-invasive and accurate imaging modalities has expanded the possibilities of managing abdominal gunshot and stab wounds. Yet, to this day, the role of ultrasonography compared with CT scan is still being clarified. An objective evaluation of CT scan for penetrating abdominal wounds showed that this imaging modality has excellent accuracy[4] of at least 94%, with 100% sensitivity and 94% specificity.[5] However, the high cost of this procedure precludes its routine use in the local setting. In addition, it is not yet readily available in many local trauma centers. Although the Philippines continues to develop its trauma care services by providing education to trauma care personnel and improving facilities, not all institutions can afford the latest advances in trauma care.

The logical alternative to CT scan may be ultrasonography. It costs less and is more widely available. In a recent meta-analysis of Focused Assessment with Sonography for Trauma (FAST), the pooled overall sensitivity and specificity of ultrasound were 78.9% and 99.2%, respectively.[6] In this regard, this study was formulated to compare the available diagnostic modalities presently being used in a 200-bed tertiary government Level II Trauma Center which caters mostly to patients from the lower socioeconomic groups. There is no CT scanner or materials for other minimally invasive procedures that may be done bedside or in the operating room for both the diagnosis and treatment of trauma patients. The only available non-invasive diagnostic test for trauma in this hospital is ultrasonography, performed for trauma patients using the FAST technique. The objective of this study was to compare the accuracy of FAST with local wound exploration in detecting intra-abdominal injury secondary to gunshot and stab wounds by calculating the sensitivity, specificity, predictive values and likelihood ratios of each diagnostic modality.

Methods

This is a cross-sectional study conducted from June 2009 to June 2011 at a tertiary government level II trauma center in Manila. Included in the study through their medical records were all patients treated for abdominal gunshot and/or stab wounds. Anterior abdominal wounds included those confined between the two midaxillary lines laterally, a line connecting the anterior costal margins superiorly and a line over the pubic symphysis inferiorly. Posterior abdominal wounds included those located between the two midaxillary lines laterally, a line connecting the tips of the scapulae superiorly and a line over the gluteal folds inferiorly. Patients who were immediately brought to the operating room for surgery without undergoing either of the test procedures were excluded.

The following data were obtained from the records:

1. Demographic profile
2. Mechanism of injury, whether gunshot or stab
3. Location of injury, whether anterior or posterior abdomen (back)
4. Diagnostic procedures and results, whether FAST, local wound exploration, or both
5. Management, whether surgical or conservative
6. Intraoperative findings, including organ/s injured, if any

Local wound exploration was performed as follows: After sterile skin preparation and infiltrating with a local anesthetic, the wound was surgically extended and inspected under direct vision. LWE was labeled as positive if the fascia was penetrated, and negative in the absence of fascial penetration. FAST was performed as follows: The patient was placed in a supine position. Using the curvilinear probe of a Medison SonoAce™ ultrasound machine, the sonologist on duty evaluated four areas of the abdomen: the perihepatic, perisplenic,

pelvic and pericardial spaces. It was labelled as positive if a black rim, representing free intraperitoneal fluid, was present between two organs, or if an abnormal black rim was found inside a solid organ, indicative of gross injury to that organ. The FAST was considered to be negative in the absence of the black rim described. The gold standard was the intraoperative findings; the subjects were categorized as positive if there was injury or negative, if none was found. In subjects who did not undergo surgical intervention, recovery without sequelae was considered negative.

The results of the FAST and LWE were compared to the results of the gold standard by calculating the sensitivity, specificity, positive predictive value, negative predictive value, and likelihood ratio with 95% confidence interval for each modality.

Results

The study included 95 subjects whose records were retrieved from June 2009 to June 2011. Their mean age was 31 years and more than 95% were males who sustained stab wounds in the anterior abdomen. More than two-thirds underwent FAST or LWE while 35 patients underwent both the FAST and LWE. A total of 78 patients had anterior wounds, with 62 (77.5%) undergoing LWE and 53 (66.2%) undergoing FAST. These are summarized in Table 1.

Table 2 compares the results of the FAST with the gold standard and shows that the FAST detected 19 of the 52 patients with injury, for a sensitivity of 36.5%, and accurately ruled out injury in all 16 patients without injury, for a specificity of 100%. The positive predictive value was 100%, and the negative predictive value was 32.7%. Positive likelihood ratio was approximated (by converting 0 to 0.5), to be 6.2 (95% CI: 0.7 – 189.2) while the negative likelihood ratio was 0.6 (95% CI: 0.2 – 0.5). Table 3 compares the results of LWE with the gold standard and shows that LWE accurately detected 38 of the 40 patients with injury, for a sensitivity of 95.0%, and ruled out injury in 11 of the 22 patients without injury, for a specificity of 50.0%. The positive predictive value was 77.6%, and the negative predictive value was 84.6%. The positive likelihood ratio was 12.1 (95% CI: 2.2 – 65.2), while the negative likelihood ratio was 0.1 (95% CI: 0.02 – 0.4). Table 4 compares the test parameters of the FAST versus LWE, with corresponding 95% confidence intervals.

Table 2. Comparison of FAST results with operative findings or conservative management in a level 2 trauma center, Manila, June 2009 - June 2011.

FAST	(+) Injury	(-) Injury	TOTAL
Positive	19	0	19
Negative	33	16	49
TOTAL	52	16	68

Table 3. Comparison of LWE results with operative findings or conservative management in a level 2 trauma center, Manila, June 2009 - June 2011.

LWE	(+) Injury	(-) Injury	TOTAL
Positive	38	11	49
Negative	2	11	13
TOTAL	40	22	62

Table 1. Characteristics of patients with abdominal stab and gunshot wounds who underwent FAST and LWE in a level 2 trauma center, Manila, June 2009 - June 2011.

Characteristic		Diagnostic Procedure		Subjects
		FAST (N=68)	LWE (N=62)	TOTAL (N=95)
Mean age (years)				31
Gender	Male	64 (94.1%)	58 (93.5%)	91 (95.8%)
	Female	4 (5.9%)	4 (6.5%)	4 (4.2%)
Mechanism of injury	Stab Wound	66 (97.1%)	52 (83.9%)	85 (89.5%)
	Gunshot Wound	2 (2.9%)	10 (16.1%)	10 (10.5%)
Location of Injury	Anterior	53 (77.9%)	62 (100.0%)	78 (83.9%)
	Posterior	15 (22.1%)	0	15 (16.1%)
Operative findings	Positive for injury	50 (73.5%)	39 (62.9%)	65 (68.4%)
	Negative for injury	3 (4.4%)	7 (11.3%)	7 (7.4%)
	Surgery not done	15 (22.1%)	16 (25.8%)	23 (24.2%)

Table 4. Comparison of the test parameters of FAST and LWE, with corresponding 95% confidence intervals in a level 2 trauma center, Manila, June 2009 - June 2011.

PARAMETER	FAST	Confidence Interval	LWE	Confidence Interval
Sensitivity	0.365	0.248 - 0.501	0.95	0.835 - 0.986
Specificity	1 (0.97)	0.765 - 0.997	0.5	0.307 - 0.693
Positive Predictive Value	1 (0.99)	0.759 - 1	0.776	0.630 - 0.878
Negative Predictive Value	0.327	0.204 - 0.477	0.846	0.537 - 0.973
Positive Likelihood Ratio	12.06	2.23 - 65.25	1.9	1.244 - 2.903
Negative Likelihood Ratio	0.635	0.516 - 0.78	0.1	0.024 - 0.411
Prevalence	0.759	0.638 - 0.851	0.645	0.517 - 0.760

In order to determine whether location of injury, anterior or posterior, could have influenced the comparison of the accuracy of the two diagnostic tests, a sensitivity analysis was done by excluding 15 patients with posterior wounds, and recalculating the accuracy. Results showed no significant change in the accuracy of the test parameters. A secondary analysis, including only the patients who underwent both FAST and LWE, was also done to determine if this could have altered the test results. Recalculation, however, showed no significant change in the test parameters.

Discussion

This study showed that FAST had a high specificity but low sensitivity, while LWE had a high sensitivity but a low specificity. FAST accurately ruled out 100% of patients with no abdominal injury, but failed to detect more than half of those with significant injury. In contrast, LWE accurately detected 95% of those with abdominal injury, but failed to rule out half of those with no injury.

There were no false positives for FAST, and calculation of the positive likelihood ratio could only be done by converting the "0" to "0.5" value. The positive likelihood ratio showed that the probability of injury was increased 12 times if FAST was positive. However, the negative likelihood ratio showed that the probability of injury was decreased only 1.6 times if FAST was negative. In contrast, the positive likelihood ratio for LWE showed that the probability of injury was increased only two times if LWE was positive, but the negative likelihood ratio showed that the probability of injury was decreased 10 times if LWE is negative.

For the predictive values, if FAST result was positive, then the probability of injury was a virtual certainty, compared with LWE, in which the probability of injury was less than 80%. However, if FAST result was negative, the probability that there was really no injury was only around 32%, as compared to almost 85% for LWE. Except for the positive likelihood ratio, the test results we obtained were moderately precise, as shown by the 95% confidence intervals and are indicative of an adequate sample size.

The results of this study indicate that the two diagnostic modalities complement each other. The weakness in accuracy of one modality is offset by the strength of the other modality. With its high sensitivity, LWE is a good screening test to determine those subjects with intra-abdominal injury. FAST can then be performed to rule out the intra-abdominal injury due to its high specificity.

A systematic review of the medical literature revealed a meta-analysis[6] that compared the accuracy of FAST among different studies. The pooled overall sensitivity and specificity were 78.9% and 99.2%, respectively. There were no differences in test accuracy between trials that included patients with penetrating injuries and those that did not. This present study, showing a high specificity but lower sensitivity for FAST, is consistent with all these. The findings agree with previous studies[1, 2] which have consistently concluded that LWE can decrease the number of negative laparotomies due to its high accuracy in detecting injury.

The Basic Emergency Skills in Trauma (BEST) course curriculum of the Philippine College of Surgeons includes LWE and FAST as options in patients with penetrating abdominal trauma who have equivocal abdominal findings and stable vital signs. Wound exploration may be utilized for a single anterior abdominal wound, with the additional stipulation of

performing diagnostic peritoneal lavage (DPL) if wound exploration proves to be positive. FAST is a good modality to determine if there is free intraperitoneal fluid or solid organ injury. However, it is operator dependent and there must be at least 50 ml of free peritoneal fluid to be sonographically visible.[7]

As a retrospective cross-sectional study, this research has several inherent limitations. Ultrasound is known to be operator-dependent and in this study, FAST was performed by several sonologists. In addition, CT scan as a gold standard was not possible since it was not available in the study site. Thus, for patients who did not undergo surgery, the authors had to rely on clinical observation and monitoring to confirm the absence of significant injury. It is also possible that some symptomatic patients may have undergone FAST and/or LWE despite indications for immediate surgery. Unfortunately, these data were missing in the patients' medical records. This could have resulted in an overestimation of the actual accuracy of the tests under study.Future studies validating this study's results should be prospective to allow better control of selection and information bias. A larger sample size can also increase the precision of the results. Additional outcomes for such a prospective study should be a comparison of complication rates and other adverse events, especially for LWE, which is an invasive diagnostic procedure. In summary, this study showed that LWE is an accurate diagnostic procedure in detecting traumatic injuries, while FAST is accurate in ruling out significant injury in patients with abdominal stab and gunshot wounds. For such patients with suspected intra-abdominal injury, LWE should be done first as a screening test followed by FAST as a confirmatory test.

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