RANDOMISED, DOUBLE BLIND CONTROLLED TRIAL ON PREOPERATIVE ANXIETY LEVEL BETWEEN PREMEDICATED AND NON-PREMEDICATED PATIENTS UNDERGOING ELECTIVE SURGERY

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ABSTRAK

Tajuk: Kajian Kawalan Dwi Sorokan Secara Rawak Untuk Menentukan Tahap Keresahan Dikalangan Pesakit Pembedahan Elektif samada Pesakit menerima Ubat Midazolam atau tidak.

Tujuan: Pesakit tidak perlu mengalami keresahan sebelum pembedahan. Kajian ini bertujuan untuk menentukan tahap keresahan yang dialami oleh pesakit pembedahan elektif.

Kaedah: Suatu pengajian kawalan dwi sorokan secara rawak untuk menentukan tahap keresahan. Pesakit telah mengisikan borang soal selidik sebelum dan selepas menerima ubat Midazolam atau plasebo. Hospital Anxiety and Depression Scale(HADS) telah digunakan, di mana empat belas soalan telah dibahagikan untuk menentukan keresahan dan kemurungan. Paired T-test untuk perbandingan dalam kumpulan dan T-test tidak bersandar antara kumpulan telah digunakan semasa analisis statistic SPSS 11.0. Nilai P kurang daripada 0.05 dianggap signifikan.

Keputusan: Seratus empat puluh set soalan selidik telah diperolehi dan tidak ada perbezaan yang signifikan secara statistik ' berdasarkan ciri-ciri demografi '. Kumpulan interventional telah memperolehi tahap purata keresahan sebelum menerima ubat ialah 8.3 ± 2.3 (min ± sisihan piawai) dan selepas menerima ubat adalah 3.3 ± 1.8 dengan nilai P = 0.001, tetapi kumpulan plasebo telah memperolehi tahap keresahan sebelum ubat ialah 8.9 ± 2.3 dan selepas menerima ubat ialah 10.24

± 2.9 dengan nilai P = 0.001. Perbezaan tahap keresahan telah dilakukan antara kaum, jantina, kelas ASA dan jenis pembedahan.

Kesimpulan: Keputusan kajian ini menunjukkan kewujudan tahap keresahan yang tinggi sebelum pembedahan dan ubat Midazolam dapat mengurangkan tahap keresahan tersebut. Kumpulan plasebo memperolehi tahap keresahan yang tinggi sebelum pembedahan dan tahap keresahan tersebut meningkat tinggi lagi pada pagi pembedahan. Kumpulan kaum perempuan, ASA kelas kedua dan pesakit puan yang menjalani pembedahan memperolehi tahap keresahan yang tinggi.

ABSTRACT

Title: Randomised, Double Blind Controlled Trial on Preoperative Anxiety Level between Premedicated and Non-premedicated Patients Undergoing Elective Surgery.

Purpose: Patients should not suffer needless anxiety before surgery. This study was aimed to determine the level of anxiety that exist in patients undergoing elective surgical procedure from various departments. Comparison was also made within the various demographical data obtained with specific objective.

Methods: This was a prospective randomized, double blind controlled clinical trial on preoperative anxiety levels. Patients completed the anxiety assessment scales both before and after intervention. The scale used was Hospital Anxiety and Depression Scale(HADS) The fourteen questions were subdivided to assess anxiety and depression separately. Paired T-test within groups and independent T-test for between groups were used during statistical analysis using SPSS 11.0. A $p < 0.05$ was considered to be significant.

Results: One hundred and forty scale sets were obtained with no statistically significant difference in demographic characteristic. The interventional group had pre-intervention mean anxiety score of 8.3 ± 2.3 (mean $\pm$ SD) and post- intervention mean anxiety score of 3.3 ± 1.8 with $p = 0.000$ where the placebo group had pre-intervention score of 8.9 ± 2.3 and post-intervention score of 10.24 ± 2.9 with $p = 0.001$. Differences were also seen in mean anxiety score with ethnicity, gender, ASA class (American Society of Anesthesiologist) and type of operation.

Conclusion: In this study, it was found that significant level of anxiety existed preoperatively and premedication reduced it's level significantly. The placebo group had the highest level of anxiety and its level increased even more immediately before surgery. In addition, female patient, ASA II and patients undergoing gynaecological surgery had higher level of anxiety.

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ABBREVIATIONS

PAC	Pre – anaesthetic clinic
SDA	Same day admission
ASA	American Society of Anesthesiologist
GAD	Generalised anxiety disorder
MAOI	Monoamine oxidase inhibitors
GABA	Gamma amino butyric acid
GAR	Gamma amino receptor
GAR C	Gamma amino receptor complex
ECG	Electrocardiogram
CNS	Central Nervous System
BP	Blood pressure
HADS	Hospital anxiety and Depression Scale
HR	Heart Rate
IV	Intravenous
IM	Intramuscular
PTSP	Post traumatic stress disorder
OCD	Obsessive compulsive disorder
C max	Mean peak concentration
T max	Time peak concentration
Vd	Volume of distribution
HUSM	Hospital Universiti Sains Malaysia
ANS	Autonomic nervous system

IVF	In Vivo fertilization
CV	Concentration volume
CI	Total clearance
REM	Rapid Eye Movement
GCS	Glasgow Coma Scale

CHAPTER ONE

Introduction

1.1 Background.

1.1.1 Overview of anxiety and surgery

Anxiety is a normal state of apprehension, tension, and uneasiness in response to a real or perceived threat. Although anxiety is considered a normal response to temporary periods of stress or uncertain situations, prolonged, intense, or inappropriate periods of anxiety may indicate an anxiety disorder.

Anxiety is a phenomenon encountered in medicine from its beginnings (Mc Cleane *et al.,* 1990). Surgical treatment involves extremely high emotional burden for the patient and is full of threats and fears. Increased anxiety may adversely affect physiological parameters, both before and during anaesthesia. Moreover, preoperative anxiety is likely to impede the postoperative course resulting in higher numbers of complications, increased post operative pain and prolonged hospitalisation. Preoperative anxiety of patients has not been sufficiently known; there are also no standards of management taking into account its causes (Fay Bound *et al.,* 2004). Although excessive anxiety may be prevented and its symptoms reduced by appropriate education and good communications with patients, prophylactic and therapeutic actions are not routinely taken.

Traditionally, patients were admitted to hospital the day before surgery. Anesthesiologist uses the in-patient preoperative visit to assess the patient's clinical and psychological state and to establish rapport. These encounters were also used to address and alleviate patients' concerns regarding their upcoming procedure. Despite the apparent benefits of in-patient preoperative visit, pre-anesthetic clinics (PAC), same day admission (SDA) for surgery as well as day surgery have now become the norm in most practice settings. These changes have resulted in patients meeting their anesthesiologist just minutes before the operative procedure. Despite these time constraints, there is still a need for the anesthesiologist to address the patients' medical and psychological concerns. New tools are needed to assist the anesthesiologist in this task. One such needed tool is a quantitative scale of preoperative anxiety.

1.2 Objective of the study

1.2.1 General Objective

To determine the level of anxiety that exists in patient undergoing elective surgical procedure.

1.2.2 Specific Objective

To compare the level of anxiety between:

- Age
- Sex
- Ethnic group
- Effect of anxiolytic

- ASA
- Type of operation

1.3 Hypothesis

There is a significant level of anxiety in patient undergoing elective surgical procedure and there is no significant difference between placebo group and interventional group receiving Midazolam as premedication.

CHAPTER TWO

Literature Review

2.1 Anxiety

2.1.1 Historical Perspective of Anxiety

Nearly a century ago, Sigmund Freud coined the term "anxiety neurosis" and with the publication of *Inhibitio, Symptoms and Anxiety in 1926,* Freud created a new theory of anxiety that accounted for both real external anxiety and neurotic internal anxiety as a response to a dangerous situation (Freud Sigmund *et al.,* 1977).

Freud identified two types of anxiety provoking situations. One situation involves overwhelming instinctual stimulations, the protype of which is experience of birth (Robert Kramer *et al.,* 1996). In situations of that variety, the excessive amount of drive pressure penetrates the protective barriers of the ego, producing a state of helplessness and trauma. The second and more common situation involves anxiety that develops in anticipating of danger (Lazarus *et al.,* 1991). That warning to the organism, known as signal anxiety, operates at an unconscious level and serves to mobilize the ego's resources of danger may produce such a signal that leads the ego to marshal specific defense mechanism to guard against or to reduce the degree of instinctual excitation(Lazarus *et al.,* 1991)

For the past 15 years, American Psychiatry Society has seen the anxiety disorders move away from concept based on psychodynamic formulations of neurosis (Bayer *et al.*, 1985). The result has been that the word "neurosis" has been dropped from the official nomenclature and the division among the various anxiety disorders has been made on the basis of valid and reliable clinical criteria (Mayer *et al.*, 2005).

2.1.2 Types of Anxiety

The sensation of anxiety is commonly experienced by virtually all humans. The feeling is characterized by a diffuse, unpleasant, vague sense of apprehension often accompanied by autonomic symptoms.

The *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR)* classifies the anxiety disorders into the following categories:

- Panic disorder
- Obsessive-compulsive disorder (OCD)
- Posttraumatic stress disorder (PTSD)
- Social phobia
- Specific phobias
- Generalized anxiety
- Anxiety due to a general medical condition
- Substance-induced anxiety disorder
- Acute stress disorder
- Adjustment disorder with anxious features

Panic disorder: People with this condition have feelings of terror that strike suddenly and repeatedly with no warning. Other symptoms of a panic attack include sweating, chest pain, palpitations and a feeling of choking, which may make the person feel like he or she is having a heart attack or "going crazy".

Obsessive-compulsive disorder (OCD): People with OCD are plagued by constant thoughts or fears that cause them to perform certain rituals or routines. The disturbing thoughts are called obsessions, and the rituals are called compulsions. An example is a person with an unreasonable fear of germs who constantly washes his or her hands.

Post-traumatic stress disorder (PTSD): PTSD is a condition that can develop following a traumatic and / or terrifying event, such as a sexual or physical assault, the unexpected death of a loved one, or a natural disaster. People with PTSD often have lasting and frightening thoughts and memories of the event, and tend to be emotionally numb.

Social anxiety disorder: Also called social phobia, social anxiety disorder involves overwhelming worry and self-consciousness about everyday social situations. The worry often centers on a fear of being judged by others, or behaving in a way that might cause embarrassment or lead to ridicule.

Specific phobias: A specific phobia is an intense fear of a specific object or situation, such as snakes, heights or flying. The level of fear usually is inappropriate to the situation and may cause the person to avoid common, everyday situations.

Generalized anxiety disorder: This disorder involves excessive, unrealistic worry and tension, even if there is little or nothing to provoke the anxiety.

2.1.3 Causes of Anxiety

The exact cause of anxiety is not fully known, but a number of factors including genetics, brain chemistry and environmental stresses appear to contribute to its development.

Genetics: Some research suggests that family history plays a part in increasing the likelihood that a person will develop generalised anxiety disorder (GAD). This means that the tendency to develop GAD may be passed on in families (Kindler *et al.*, 1992).

Brain chemistry: GAD has been associated with abnormal levels of certain neurotransmitters in the brain. Neurotransmitters are special chemical messengers that help move information from nerve cell to nerve cell. If the neurotransmitters are out of balance, messages cannot get through the brain properly. This can alter the way the brain reacts in certain situations, leading to anxiety (Murray *et al.*, 2007).

Environmental factors: Trauma and stressful events such as abuse, the death of a loved one, divorce, changing jobs or schools may lead to GAD. GAD may also worsen during periods of stress. The use of and withdrawal from addictive substances including alcohol, caffeine and nicotine can also worsen anxiety (Hettema *et al.*, 2005).

2.1.4 Pathophysiology of Anxiety

Heightened physiologic response and elevated catecholamines levels play an important role in the normal physiologic response of the body to stress and anxiety. It has been hypothesized that pathologic anxiety results from disturbances in the cerebral cortex specifically the limbic system (David *et al.*, 1992). The neurotransmitters

primarily associated with anxiety in these regions are norepinephrine, gamma-aminobutyric acid (GABA), and serotonin. The efficacy of benzodiazepines in treating anxiety has implicated GABA in the pathophysiology of anxiety disorders (Goddard *et al.*, 2001). Drugs that affect norepinephrine (eg, tricyclic antidepressants, monoamine oxidase inhibitors [MAOIs]) are also efficacious in the treatment of several anxiety disorders. Recent advances have demonstrated the benefit of serotonin in anxiety and panic attacks (Nutt *et al.*, 1998).

2.1.5 System Effects of Anxiety

Nervous System: When some sort of danger is perceived or anticipated, the autonomic nervous system is stimulated. The autonomic nervous system has two subsections or branches namely, the sympathetic nervous system and the parasympathetic nervous system. The sympathetic nervous system is the 'fight/ flight system' which releases energy and gets the body "primed" for action while the parasympathetic nervous system is the restoring system which returns the body to a normal state.

Cardiovascular: Activity in the sympathetic nervous system produces an increase in heart rate and contractility. This is vital to preparation for activity since it helps speed up the blood flow, thus improving delivery of oxygen to the tissues and removal of waste products from the tissues.

In addition to increased activity in the heart, there is also a change in the blood flow. The blood is moved to the large muscles such as the thighs and biceps, which help the body preparing for action.

Respiratory System: The fight/ flight response is associated with an increase in the speed and depth of breathing. This has obvious importance for the defence of the organism since the tissues need to get more oxygen in order to prepare for action. The effects produced by this increase in breathing, however, can include breathlessness, choking or smothering feelings and even pains or tightness in the chest. A side effect of increased breathing, especially if no actual activity occurs, is that blood supply to the head is actually decreased. While this is only a small amount and is not at all dangerous, it produces a collection of unpleasant but harmless symptoms including dizziness, blurred vision, confusion, unreality and hot flushes (Seligman *et al.*, 2001).

Digestive system: There is a decrease in salivation, resulting in a dry mouth as well as decreased activity in the digestive system, which often produces nausea, a heavy feeling in the stomach and even constipation. Many of the muscle groups tense up in preparation for fight or flight and this result in subjective feelings of tension, sometimes extending to actual aches and pains as well as trembling and shaking.

Mental system: The number one effect of the fight / flight response is to alert the organism to the possible existence of danger. Thus, one of the major effects is an immediate and automatic shift in attention to search the surroundings for potential threat. For this reason, it becomes difficult for the person to concentrate on other daily tasks when he / she is experiencing anxiety attacks.

Behavioural system: The fight / flight response prepares the body for action - either to attack or to run. When this is not possible (due to social constraints), the urges will often be shown through such behaviours as tension, guilty, shivering, improper