An-Najah National University

Faculty of Graduate study

The clinical effectiveness of the Bispectral Index (BIS) to reduce the incidence of awareness for elective surgical patients undergoing general anesthesia.

A prospective, randomized, double-blind, controlled study

By
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Supervision
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Dedication

I dedicate this thesis to my precious family members.

I also dedicate this work to the spirit of the martyrs of Palestine and to prisoners of freedom in Israeli jails, and for every anesthesiologist and every CRNA nurse who has taught me as a CRNA student.

Acknowledgement

I am grateful to God for the good health and well-being that was necessary to complete this thesis. Without faculty and colleagues this thesis would not have been possible. Although it would be impossible to name individually all of the people and the events that contributed to the success of this project and the accomplishment of a remarkable educational and experiential milestone, I know and value and appreciate each and every one.

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I would like to thanks An- Najah National University Hospital for enabling me to conduct my study in its hospital.

Last but not least, my deepest gratitude for everyone who contributed to this work, I appreciate their efforts.

الاقرار

انا الموقعة ادناه مقدمة الرسالة التي تحمل العنوان:

The clinical effectiveness of the Bispectral Index (BIS) to reduce the risk of awareness for elective surgical patients undergoing general anesthesia in Nablus district

A prospective, randomized, double-blind, controlled study

أقر بأن ما اشتملت عليه هذه الرسالة انما هي نتاج جهدي الخاص، باستثناء ما تم الإشارة اليه حيثما ورد، وان هذه الرسالة ككل، أو أي جزء منها لم يقدم لنيل أي درجة أو لقب علمي أو بحثي لدى أي مؤسسة تعليمية أو بحثية أخرى.

Declaration

The work provided in this thesis, unless otherwise referenced, is the researcher's own work and has not been submitted elsewhere for any other degree or qualification.

Student name: **الاسم:**

Signature: **التوقيع:**

Date: **التاريخ:**

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List of Abbreviations

AD	Anesthesia Departments
ASA	American Society of Anesthesiologists
BIS	Bispectral Index
COPD	Chronic Obstructive Pulmonary Disease
DBP	Diastolic Blood Pressure
End tidal CO2	carbon dioxide partial pressure (mm Hg) during expiration
EEG	Electroencephalography
EMG	Electromyography
FDA	Food and Drug Administration
GA	General Anesthetic
HR	Heart Rate
IV	Intravenous
LTM	Long Term Memory
MAC	Monitored Anesthesia Care
MAP	Mean Arterial Pressure
NMDA	N-Methyl-D-Aspartate
PACU	Post Anesthesia Care Unit
PTSD	Post Traumatic Stress Disorder
RR	Respiratory Rate
SBP	Systolic Blood Pressure
SPO2	peripheral capillary oxygen saturation
Temp	Temperature

The clinical effectiveness of the Bispectral Index (BIS) to reduce the incidence of awareness for elective surgical patients undergoing general anesthesia. A prospective, randomized, double-blind, controlled study

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Abstract

Background: Unintended intra-operative awareness is a serious complication of general anesthesia. The incidence of such awareness has been reported to be about 0.1-0.6% of patients under general anesthesia. Reminiscence of what occurred during the operation can be felt by patients, which can be stressful and leave lasting mental suffering afterward the operation. Patients that experience unintended intra-operative awareness may have some combination of auditory function, tactual feeling, a sense of weakness, an inability to move, pain, and dread. Bispectral Index (BIS) monitoring has been shown to decrease awareness and boost recovery time from anesthesia. Aims of the study is to evaluate the clinical impact of BIS monitoring to reduce the incidence of awareness and its impact on hemodynamic parameters, drug consumption, the recovery time and the end-tidal concentration of volatile anesthetics in adult patients undergoing various types of surgery under general anesthesia.

Methods: The design adopted for this study is a prospective, randomized, double blind trial. The study involved fifty-nine adult patients with American Society of Anesthesiologists (ASA) physical status I-III, aged 18 to 72 years. 41 males and 18 females scheduled for different types of

operations under general anesthesia participated in the study. Patients were randomized for inclusion in the BIS-handled anesthesia group (n=30), with the BIS value controlled between 40 and 60, which is considered convenient for surgical anesthesia; or the routine care (RC) group without BIS-control (n=29). A BIS sensor was placed on the forehead of patients. Hemodynamic specifications were recorded before induction of anesthesia and every five minutes during surgery until the removal of the endotracheal tube. The patients were interviewed by a blinded observer at 24-36 hours after operation through the use of a structured questionnaire. Two independent endpoint adjudication committees blinded to group identity assessed the interview results and identified the confirmed awareness cases.

Findings: There were no significant differences between the two groups in all the general characteristics of the patients. Regarding anesthetic time, the mean ± SD in the RC group was 76.6 ± 84.3 minutes, and 124.2 ± 124.4 minutes in the BIS group; the difference was not significant. Surgical time was 73.8 ± 85.8 minutes in the RC group and 116.4 ± 106.2 minutes in the BIS group; the difference was not significant. Of the total 59 patients 29 patients were assigned to the routine control group and 30 patients to the BIS group. No case of awareness was reported in the BIS-guided group but 4 reports (13.8%) in the control group (P=0.035), BIS-guided anesthesia decreased awareness by 13.8% (95% CI (1.3%-26.4%). The most common forms of awareness was auditory perceptions, tactile perception and the sense of paralysis.

There was a statistically significant difference in the mean dose of inhaled anesthetic agents between the RC group (0.029 ±0.008 %) and the BIS group (0.025 ± 0.009%), P=-0.023, which indicates that BIS monitoring could reduce the needed use of inhalation anesthesia. Regarding the opioid fentanyl there was also a significant difference in the used dose of fentanyl for the BIS group (115.56 ± 94.18 mcg and the RC group (77.76 ± 40.52 mcg), P=0.035.There was found to be a difference in the propofol dosage between the BIS group (474.07 ± 711.3 mg) and the RC group(230 ± 59.938 mg), P=0.235. It is clear that patients in the RC group had a lower dosage of propofol than patients in the BIS group, but the difference was not significant. Low doses of fentanyl and propofol may be one of the causes of awareness in the RC group. We found no significant differences in somatic responses of sweating, tearing, pupil dilation and coughing intra-operatively between BIS-monitored and RC patients. However, a significant reduction in intra-operational jerking was recorded for the favor of BIS group .The percentage of patients who experienced jerking movements intra-operatively was 27.6% in the RC group and 6.9% in the BIS group, P=0.037.

There were no statistically significant differences between the two study groups in any of the time measures under study which are: time from cessation of inhalational agents to eye opening; time to respond to commands; time to eye opening (either spontaneously or in response to command, time to first movement response; and time to extubation. The time to phonation for the RC group was 12.82 ± 6.11 minutes and only

10.21 ± 5.127 minutes for the BIS group, P=0.026, this occurs for the favor of BIS group.

There is a statistically significant difference between the two groups in the time to discharge from the PACU at 12.38 ± 4.989 minutes for the RC group and 9.23 ± 3.819 minutes for the BIS group, P=0.007. In other words, patients in the BIS-monitored group were discharged earlier from the Post Anesthetic Care Unit (PACU) than the RC patients.

Conclusions: BIS-guided anesthesia where the BIS score is kept between 40 and 60, reduced the risk of awareness compared to routine care. The main reason for the occurrence of awareness in the RC group could be due to a light general anesthetic. In addition, BIS monitoring reduces the usage of volatile anesthesia and the time of discharge from the Post Anesthetic Care Unit.

Keywords

Awareness; General anesthesia; BIS; Monitoring

Chapter One

1.1 Introduction

Anesthesia can be defined as a state of drug-induced unconsciousness in which the patient does not perceive or remind noxious stimulation (CPrys-Roberts, 1987). Awareness is postoperative memory of the events that develop during anesthesia (Myles, et al. 2000; Sandin, et al. 2000). It is crucial that the level of anesthesia (GA) is suitable for the individual patient undergoing surgery. If anesthesia is deeper than needed to keep a patient unconscious, it can incline the risk of anesthesia-related morbidity, such as postoperative nausea, vomiting, and cognitive dysfunction that can extend recovery time, and increased health care costs. If anesthesia is too light, patients cannot be fully unconscious and may be at fortune for intra-operative awareness. Intra-operative awareness is a rather rare event with an incidence of about 1-2 patients / 1000. Awareness is known to instigate depression, anxiety and post-traumatic stress disorder (PTSD) postoperatively (Lyons & Macdonald, 1991).

Under general anesthetic (GA), the patient is routinely monitored for signs of potential intra-operative awareness, including tachycardia (rapid heart rate), high blood pressure, sweating, lacrimation (tear production), motion / grimaces and tachypena (rapid breathing). In patients receiving inhaled GA, end-tidal (exhalation) can be assessed by anesthetic gas concentrations to measure the depth of anesthesia. But clinical observation alone is not a reliable marker for the depth of anesthesia. Technologies have been

developed using electroencephalography (EEG) for measuring and interpreting electrical activity of the brain to provide a measure of consciousness. Most EEG units include a module that collects and analyzes raw data from sensors placed on the patient's forehead. Output is then displayed numerically on a monitor for use by the anesthetist to assess the depth of unconsciousness. One of these EEG devices is the Bispectral Index (BIS) (Todd, 1998, O'Connor, 2002 Kalkman, 2002).

The aim of this study is to evaluate the clinical effectiveness of BIS monitoring and its relevance to hemodynamic parameters, drug consumption, incidence of awareness, recovery times, and end-tidal volatile anesthetic concentration in adult patients undergoing different types of surgery under general anesthesia.

Definition of study concepts

Awareness

Awareness is defined as an explicit memory from the anesthesia period during which the patient should have been, and in most cases was regarded to be, unconscious. Awareness is an experience that patients, when questioned, have regarded as the most dissatisfactory event during the peri-operative period (Myles, et al. 2000).

Incidence of awareness

In three large studies, conducted over the past ten years and in different parts of the world indicated the incidence of awareness has been reported to be about 0.1-

0.2% (Myles, et al. 2000, Sandin, et al. 2000, Sebel, et al. 2004). However in two recent studies somewhat higher incidences of awareness (0.4%, and 0.6%, respectively) were found (Errando, et al. 2008, Xu, et al. 2009).

In a report using data from a questionnaire intended for quality assurance in the postoperative period, the incidence of awareness was found to be as low as 0.0068% (Pollard, 2007).

Pollard study was, however, not designed to detect awareness and the study interview tool omitted questions pertinent to determining awareness.

(Pollard, 2007).

The risk of experiencing awareness is reported to be increased in patients undergoing heart surgery, Caesarean section surgery to repair traumatic injury, and in patients with a history of long-term use of opioids and benzodiazepines, and or who consume alcohol daily (Ghoneim, 2007). However, it has been shown that it is possible to reduce the incidence of awareness even in “high risk surgery cases”, implying that the increase in awareness could be related to the anesthetic technique rather than to the type of surgery (Paech, et al. 2008).

Detection of awareness

It has become a well-known fact that patients who have experienced awareness are reluctant to talk about it, if not directly asked. Interview methods for detecting experiences of awareness have been developed, first by Brice, et al. (1970) and later modified by Liu (1991).

The modified Brice interview has been widely adopted and is now used in most studies for detecting awareness.

Major and minor criteria of awareness

Major criteria to detect awareness

• Preoperative long-term use of anticonvulsant agents

• Opiates, benzodiazepines, or cocaine

• Heavy alcohol intake

• History of anesthesia awareness and/or history of difficult intubation

• ASA physical status class IV or class V (Appendix VIII)

• Aortic stenosis

• Pulmonary hypertension

Minor criteria of awareness

- Use of beta-blockers
- Chronic obstructive pulmonary disease (COPD)
- Smoking two or more packs of cigarettes per day
- Obesity BMI > 30

BIS as a tool for measuring sedation

The most recent update on the history and current uses of BIS monitoring was published in 2006 (Johansen, 2006). The BIS monitor is essentially a

modified EEG that can reflect the decreased cerebral metabolic rate caused by anesthetic agents (Kelley, 2010). It was first introduced in 1996 to help monitor cortical function during hypnotic states and in 2003 it was approved by the Food and Drug Administration (FDA) for reducing the incidence of intraoperative awareness (Johansen, 2006; Kelley, 2010). BIS values are measured on a scale of 0 to 100. A value of 0 indicates complete cortical suppression (i.e., an isoelectric EEG signal) and a value of 100 indicates the patient is awake (Johansen, 2006, Kelley, 2010). In actuality, values of 93 or above indicate a state of wakefulness (Johansen, 2006). Sedation is said to occur with BIS values between 65 and 85, and GA occurs between values of 45 and 60 (Johansen, 2006).

The Bispectral index (BIS) is an empirically derived algorithm that reflects the state of the brain in relation to sedation. Bispectral index (BIS) is frequently used as a monitor in the operating room to measure the depth of anesthesia and to help guide the titration of medications during general anesthesia (GA) (Hata et al., 2009). The BIS seems to function well as a practical clinical on-line trend monitor of the level of sedation.

Bispectral index (BIS) is frequently used as a monitor in the operating room to measure the depth of anesthesia and to help guide the titration of medications during general anesthesia (GA). Although there are some studies in that have looked at the use of BIS as an adjunctive monitor for titrating a patient's sedation level with sedatives and anxiolytics (Bell, et al. 2004; Drake, et al, 2006; Hata, et al. 2009), there is limited research that

has evaluated BIS values in patients undergoing sedation given by anesthesia.

1.2 Problem Statement

Posttraumatic stress disorder appears in 33-56% of patients who experienced awareness during general anesthesia. Depression, anxiety, sleep disturbances, nightmares, and panic attacks may appear 2 years and more after experiences of awareness during GA. The incorporation of paralytic agents into the administration of general anesthetics was associated with an epidemic of cases of awareness, as anesthesiologists discovered that these agents did not diminish consciousness in any way. The practice of anesthesia has evolved during the past 50 years, with increasingly safer agents, increasingly reliable monitoring, and increasing scientific understanding of general anesthesia (Vandam, 1997).

However, in recent years, there has been increased attention to the problem of unexpected recall during general anesthetics. The Bispectral Index (BIS) monitor (Aspect Medical Systems, Natick, MA) has been advocated as a tool that may reduce the incidence of unexpected recall (Ranta, et al.1998; Samuelsson, et al., 2007; Osterman, et al. 2001; Sammartino, et al. 2010). Bispectral (BIS) monitoring is one of the recent techniques proposed to monitor the depth of anesthesia and measures sedation, hypnosis and loss of consciousness (Rosow, et al. 2001, Akcali, et al. 2008, Sandlin, et al. 2001, Ishizawa, et al. 2007). By maintaining the BIS index between 40 and 60, the recommended value for general

anesthesia, a reduction of anesthetic requirement and shorter length of stay in post intensive care unit can be predicted (Recart, et al. 2003). Because of its monitoring efficacy, BIS is now intended to replace other monitoring systems for classifying the depth of anesthesia. The important characteristic of this indexing system is its ability to titrate used anesthetic agents within general anesthesia allowing anesthetists to adjust the amount of anesthetic agent to the needs of patient (Choi, et al. 2013). This might result in a more rapid emergence from anesthesia as well as reducing the incidence of intra-operative awareness in surgeries. This study will address the main question: Does bispectral index (BIS) reduce awareness for patients who are undergoing different types of elective surgeries under general anesthesia in Nablus district?

1.3 Significance of the study

Anesthesia: is a state in which the patient feels no pain. This may range from blocking the sensation of one small part of the body to total unconsciousness. Awareness while under general anesthesia, and the later recall of what happened during surgery, can be experienced by patients as horrific events that leave lasting mental trauma behind. Patients may have both auditory and tactile perception, potentially accompanied by feelings of helplessness, inability to move, pain, and panic ranging to an acute fear of death. For some patients, the experience of awareness under anesthesia has no squealae; for others, however, it leads to the development of post-traumatic stress disorder, consisting of complex psychopathological

phenomena such as anxiety, insomnia, nightmares, irritability, and depression possibly leading to suicide (Moerman, et al.1993).

Awareness is an uncommon complication of anesthesia occurring in 0.1-0.2% of all surgical patients (Myles, et al 2000). Bispectral index (BIS) monitoring measures the depth of anesthesia and facilitates anesthetic titration that could quantify the level of awareness of the patient. In Palestine, we do not have enough information about the incidence of awareness in various types of surgery under general anesthesia. It is our belief that such a tool can reduce risks in daily medical practice by helping the anesthesiologist to choose the best hypnotic dose and monitoring system in advance. Added to it this is the first study of BIS monitoring and intra-operative awareness in Palestine. This study will be a reference guide for anesthesia teams and the outcomes of this study may have an implication on patient safety, mental health, reduction of medical-legal issues, and economical outcomes for the patients and health system implications.

1.4 Aim of the study

The aim of this study is to evaluate the clinical effectiveness of BIS monitoring to reduce the incidence of awareness and its relevance to hemodynamic parameters, drug consumption, recovery times and end-tidal volatile anesthetic concentration in adult patients undergoing different types of surgery under general anesthesia.

1.5 Objectives

1. To determine whether the incorporation of BIS in clinical practice for the management of anesthesia will reduce the risk of intra-operative awareness and recall in surgical patients undergoing general anesthesia.

2. To investigate if BIS monitoring reduces drug consumption, the recovery time, and end-tidal volatile anesthetic concentration for patients undergoing general anesthesia.

3. To identify any risk or harm of BIS monitoring to patients undergoing general anesthesia.

4. To compare between BIS measures and RC groups.

1.6 Hypothesis

1. There is significant difference at a level of ≥ 0.5 related to the intraoperative awareness rate among patients undergoing BIS- guided management during general anesthesia compared with patients under routine monitoring .

2. There is significant difference at a level of ≥ 0.5 related to the time taken to recover from anesthesia as measured by the time to eye opening, is longer in routine control group compared than the BIS-group.

3. The recovery time to discharge from the PACU in the BIS group lower than the routine care group.

4. The eligibility for discharge from post anesthesia care unit as discharge criteria score (Aldrets Score) in BIS group lower than the routine care group.

5. There is significant difference at a level of ≥ 0.5 related to consumption of inhalation anesthetic agents among patients in BIS monitoring the use of BIS monitoring can shorten the time for awakening after general anesthesia and reduce consumption of inhalation anesthetic agents

Chapter Two
Literature review

2.1 Background

This chapter will discuss the definition of Bispectral Index, the means by which the BIS is calculated, the procedure used for BIS monitoring, and definition of awareness recall during general anaesthesia.

2.2 Bispectral Index definition

The Bispectral Index (BIS) is the term used most widely for monitoring brain technology to assess depth of anesthesia intraoperatively for patients. The Bispectral Index is a statistically based index, that includes a combination of frequency domain, time domain, and high-order spectral sub parameters. The BIS uses algorithm that was derived by recording EEG wave data from healthy patients who underwent transition periods between unconsciousness and consciousness after administration of several different anesthetic methods (simon.2003).

The raw EEG data were time-stamped at various clinical end points, and a multivariate logistic regression was used in offline analyses to identify the features of the EEG recordings that best correlated with clinical depth of sedation/anesthesia. The data were then fitted to a model (Sammartino, et al, 2010).

The Bispectral Index integrates several disparate descriptors from a single channel of frontal EEG into a single variable. Furthermore, with use of two frontal leads, the BIS monitor allows simultaneous assessment of bilateral

EEG activity. The BIS monitor generates a dimensionless number on a continuous scale of 0 to 100, with 100 representing alert cortical electrical activity and 0 indicating cortical electrical silence. Validation studies have demonstrated that a BIS value between 45 and 60 (optimal target) is considered suitable for surgical anesthesia and reflects a decreased cerebral metabolic rate and a very low probability of consciousness. In addition to displaying the BIS index, the monitor shows a signal quality index and an indicator of electromyography (EMG) interference, which helps the operator detect erroneous readings resulting from insufficient or inappropriate signals. As with any physiologic signal, BIS is subject to interference and artifact, particularly from EMG activity, which can elevate the recorded BIS artifact ally. Furthermore, BIS is a cortical function indicator that does not reflect the direct activity of the sub cortical structures (including the spinal cord) that primarily mediate motor response to a noxious stimulus. Thus, BIS may not be reliable for predicting movement due to noxious stimuli. Several other factors have been reported to result in inaccurate BIS readings, including the presence of senile dementia, ketamine, or esmolol (Rosow et al, 1998).

2.3 BIS calculation:

a) The BIS monitor fragments the EEG signal and identifies the artifacts.

b) The BIS monitor uses an algorithm, previously discussed, to calculate the index of the state of sedation due to changes induced by anesthetics.

c) The BIS monitor obtains the data by means of a sensor placed on the patient's forehead.

BIS-index is a number between 0 (absence of brain activity, EEG isoelectric), and 100 (patient awake). An optimal value for the maintenance of the anesthesia should be between 40 to 60 (Struys, et al. 2001)

2.4 BIS monitoring advantages:

1. Regulate anesthetic drug use.
2. Decrease the incidence of post-operative side effects such as nausea and vomiting.
3. Reduce length of stay in the PACU (recovery room).
4. Prevent intra operative awareness (Struys et al, 2001)

Table 2.1: Depth of sedation as measured by the Bispectral index system (Johansen and Sebel 2000).

Bispectral index system value	Depth of sedation
0	Flat-line EEG
0-40	Deep hypnotic state; memory function lost; increasing burst suppression
40-60	Recommended range for general anesthesia
60-90	Recommended range for sedation
100	Awake; memory intact

2.5 Mechanism of Action of Anesthesia:

General anesthesia is usually composed of a combination of hypnotics and analgesics, and when needed, muscle relaxants and/or cardiovascular drugs to regulate somatic and autonomic responses (Franks. 2008).

The mechanism of action of the most commonly used class of analgesics, opioids, and muscle relaxants, is well understood. The mechanism of action of hypnotics both inhaled and intravenous agents, is less well understood. These hypnotic agents are very diverse but they all, by definition, cause unresponsiveness and unconsciousness. Notably, the loss of consciousness (LOC) occurs abruptly over a small change in concentration (Franks, 2008).

Previously it has been thought that the effects from both inhaled anesthetic agents such as sevoflurane, and intravenous agents, such as propofol and barbiturates, were achieved by disruption of lipid bilayers or nonspecific action. These theories have been abandoned, and it is now thought that most hypnotics exert their effect by binding directly to specific protein targets (Franks, 2008). Among the known proteins, $GABA_A$ receptors are regarded as an important target for intravenous agents and to some extent also for inhaled hypnotics. Other receptors found to be of importance are two-pore-domain K+ channels, N-methyl-D-aspartate (NMDA) receptors and glycine receptors (Franks, 2008).

Anesthetics bind preferentially to preformed cavities on the proteins. The binding affects receptor function and neuronal activity and is correlated to a

dose dependent alteration of consciousness (Alkire, et al. 2008). At higher doses the patient becomes unresponsive and is regarded to be unconscious.

2.6 The administration of anesthesia

Anesthesia is used to decrease sensitivity to pain of patients undergoing surgical procedures. For different surgeries, general anesthesia and local anesthesia are applied to make patients totally or partially lose consciousness. Only general anesthesia is considered in this research. General anesthesia is administered in three phases: induction, maintenance and emergence. The descriptions of anesthetic type and process are introduced in Table 2.2.

Table 2.2: Anesthetic type and process (Tai Nguyen-Ky, 2011).

	Name	Descriptions
Type	General anaesthesia	It affects the whole body and leads to a loss of consciousness.
	Local anaesthesia	It temporarily blocks the sensation of pain in a certain part of the body while the patient remains awake
Process of general anaesthesia	Induction	The initial state of unconsciousness.
	Maintenance	Keeping patient unconscious.
	Emergence	Patient emerges from unconscious into awake.

2.7 Anesthetic Drugs

From 1840 to 1860, nitrous oxide, ether and chloroform were introduced as anesthetic drugs. At the end of the 1890s, ethyl chloride was used for the first time. After1920, the number of anesthetic agents increased markedly. Ethylene, vinethene, pentobarbital, cyclopropane, trichlorethylene, thiopental, isopropenyl vinyl ether, propylmethyl ether, meperidine, fluroxene, althesin, ethylvinylether, halothane, methohexital, droperidol, methoxyflurane, ketamine, enflurane, isoflurane, etomidate, fentanyl, midazolam, sevoflurane, alfentanyl, sufentanil, propofol, desflurane, remifentanil and xenon were introduced as anesthetic agents in succession in the 20thcentury (Urban & Bleckwenn, 2002). Currently, the propofol, midazolam, fentanyl and alfentanil are still widely used for modern general anesthesia.

Anesthetics agents are formulated for administration in three ways: inhalation (gases), injections (solutions) and topical application (see Table 2.3). Generally, the gases and injections are used for general anesthesia.

Table 2.3: Anesthetic agent administration

Type	Descriptions
Injection	The drug is injected into muscle, vein (intravenously) or under the skin with a needle.
Gases	The drug is applied with a gas mask for inhalation.
External application	Creams, gels, liquids are applied directly onto the body tissues being treated.

The most commonly used anesthetic protocol is to induce anesthesia intravenously, then maintain the anesthetized state with anesthetic gases (Tai Nguyen-Ky, 2011). Hypnotics, analgesics and muscle relaxants are typically applied together in general anesthetics. Before anesthetic agents are prepared for patients, several important factors about the drugs must be considered: concentrations with respect to each other, mechanism of administration (bolus or continuous intravenous dose) (Urban & Bleckwenn, 2002). The types and doses of anesthetic agents used for different patients are determined by anesthetists based on their knowledge base and experiences.

Figure 2.1shows the relationship between conscious and unconscious .

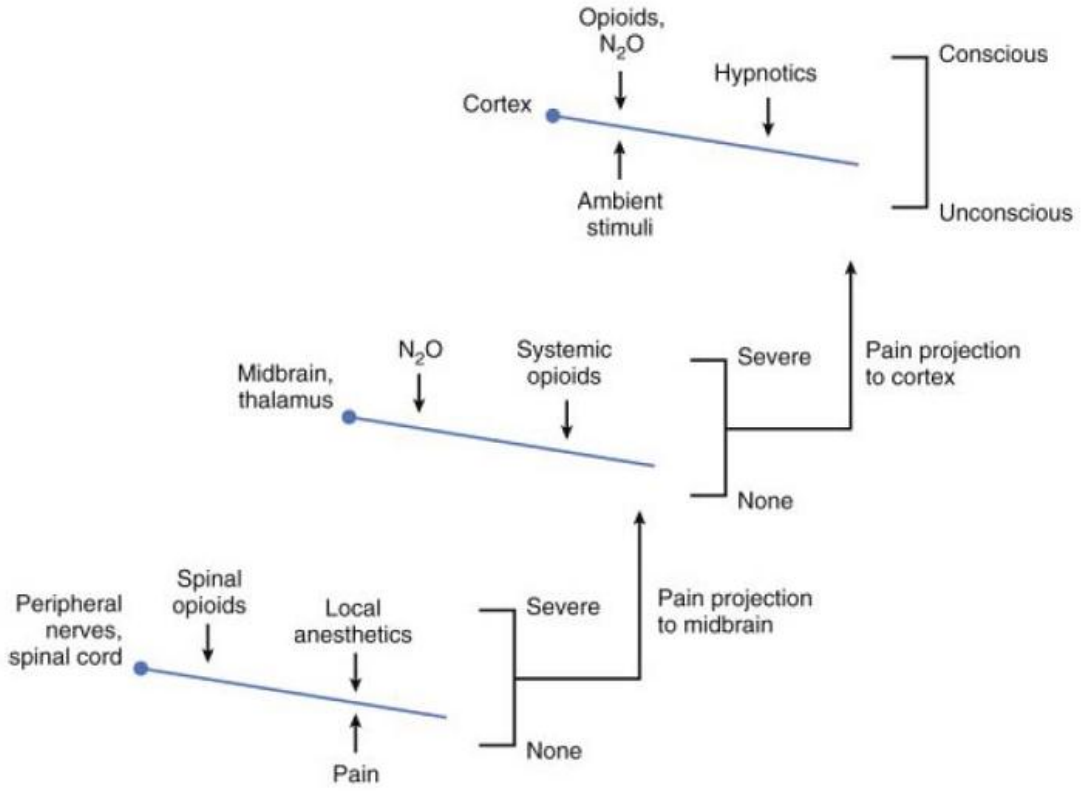

Figure 2.1: Hierarchical model of the interaction between pain and anesthetic agents to achieve unconsciousness (Gelb et al, 2010).

The Hierarchical model introduced by Gelb et al. (2010) describes anesthesia as a hierarchical system in which anesthetic agents operate at three distinct levels in the nervous system. When a patient is under dosed, there is not enough anesthetic or analgesic to prevent consciousness during the operation process. This leads to awareness during surgery (Brice, et al.1970). Intra-operative awareness occurs in 0.1% of cases in low risk procedures (Jones & Aggarwal, 2001; Myles et al. 2004; Sandhu & Dash, 2009) and 4% of cases in high risk procedures (Tonner & Bein, 2006).

Moreover, the incidence of intra-operative awareness may be over 40% for patients undergoing surgery for multiple trauma, patients undergoing

Caesarean section or cardiac surgery and patients who are hemodynamically unstable (Davidson, et al, 2005; Tai Nguyen-Ky, 2011).

When intra-operative awareness occurs, patients may feel pain or pressure , hear conversations, or feel they cannot breathe. As a result, intra-operative awareness may cause severe postoperative psychosomatic dysfunction. Therefore, intra-operative awareness is treated as a medico-legal liability for anesthetists (Sebel, et al, 2004).

2.8 Awareness

The term represents the state of mind at a certain moment of time irrespective of whether that state is later recalled or not. However, Jones and Konieczko, (2002) claim that there are different stages of "conscious awareness" and that "unconscious awareness" is also possible. In medical terminology, the term "awareness" has sometimes been regarded as meaning only consciousness during general anesthesia. This usage is different from both the general meaning of the term and its meaning in the context of psychological research. (Ghoneim, 2001)**.**

2.8.1 Awareness recall during general anesthesia:

The experience of awareness with recall during general anesthesia requires general anesthesia and awareness being present in the patient simultaneously. Furthermore, it is required that the patient later recalls the incident. It is claimed that anesthetic agents prevent the occurrence of awareness with recall by three mechanisms: 1. by interfering with the

development of neuronal adequacy for signal processing, 2. by interfering with the establishment of the time marker for the sensory experience thus distorting the experience, and 3. by interfering with recall of the conscious experience. Always rely on memory for evidence of what has been perceived during general anesthesia. This evidence, when negative, will always be somewhat equivocal. Accordingly, it is not unequivocally possible to discriminate between patients who have or have not been 'aware' or conscious during general anesthesia. The term 'wakefulness' has been used to describe patients who are able to react meaningfully to stimuli during general anesthesia but are not able to recall either the stimuli or their reactions postoperatively. There is evidence that a large number of such patients exist. There is also some evidence that wakefulness without explicit recall might be detrimental for the patient but this has not been definitely proven (Radovanovic, 2011).

The primary characteristics of awareness vary between published reports. In a study of 26 patients with intra-operative awareness Moerman et al. (1993) found that the most common form of recall was hearing sounds, reported by 89 % of the patients. Paralysis was the second most common feeling, recalled by 85 % of the study population, while pain was reported by 39 % of those included in the study. Cobcroft, and Forsdick (1993) found pain to be the most common recollection reported by 39 % of patients experiencing recall inter-operatively. Recollection of sounds was reported by 31 % of this study population. Schwender et al (1998) reported auditory perceptions to be the most common sensory modality during intra-

operative awareness (100 % of patients). The next most common feelings were tactile perceptions (64 %), and paralysis (60 %), and pain (24 %). In a closed-claims analysis (Domino et al, 1999)., auditory perception was recalled by 30 % of the study population, tactile perceptions by 25 %, pain by 21 %, and paralysis by 20%.

Awareness during anesthesia is a serious complication with potential long-term psychological consequences. Use of the Bispectral index (BIS), developed from a processed electroencephalogram, may decrease the incidence of anesthesia awareness for patient.

2.9 Studies of awareness during anesthesia

Igor Kagan, (2008) demonstrated that awareness and recollection of surgical events under general anesthesia is an adverse reaction that can lead to psychological disorders including posttraumatic stress disorder. It is estimated that 0.1% to 0.2% of patients who undergo general anesthesia in the United States are aware of their surroundings and events at some point during their surgery. Awareness under general anesthesia cannot always be fully prevented. A patient may become aware for a number of reasons including: level of anesthesia, type of anesthetic drugs, inadequate monitoring, and anesthesiologist error. However, steps may be taken to reduce the risk of awareness. The BIS monitor appears to be a promising tool to aid in reducing intra-operative awareness. But, more research is needed to quantify this promising technology.

Kotsovolis & Komninos (2009) mentioned that awareness during surgery is a very serious problem for the anesthetist as well as the patient. Awareness incidents are the cause for 2% of the legal claims against anesthetists and patients who experience intra-operative awareness describe it as the worst thing they have ever suffered from. Pain, anxiety and inability to react due to muscle paralysis often lead to the situation called posttraumatic stress disorder which demands psychiatric support. The fact that there are patients who report intra-operative experience, even several days after surgery, raises questions about the manner in which anesthetic drugs interfere with the mechanisms of memory and consciousness. Studies have proven that even deeply anesthetized patients can be influenced by auditory stimuli without being able to recall them. Intra-operative monitoring of the anesthesia depth is important for the prevention of this problem. Among all available intra-operative monitoring devices only the Bispectral Index Monitor (BIS) has been proven to be effective for this purpose. However, the high cost for this monitoring system and the low specificity in preventing awareness episodes do prevent its everyday use.

Radovanovic (2011) describes anesthesia awareness (AA) as postoperative recall of events experienced under general anesthesia. Most frequently, patients remember an auditory perception, the feeling of motor function loss, pain, helplessness, anxiety, panic, impending death. The prevalence of awareness in non-obstetric and non-cardiac surgical cases is 0.1%-0.2%. The prevalence is higher in cardiac and obstetric surgeries, and in cases of major trauma. Many studies show that under dose anesthesia is the most

common cause of AA. Posttraumatic stress disorder appears in 33%-56% of patients who experienced awareness during general anesthesia. Extreme awareness experiences are very uncommon, but traumatic, and can have lasting effects on patients. Several brain-function monitors, based on the processed electroencephalogram or evoked potentials, have been developed to assess anesthetic depth. Measures to prevent awareness include avoidance of light anesthesia, increasing the knowledge base about patient anesthetic requirements and development of methods to detect consciousness during anesthesia.

Samuelsson, et al. (2007) conducted a study of late psychological symptoms after awareness among surgical patients. The authors used prospective consecutive collection to recruit patients with previous awareness. In a cohort of 2,681 consecutive patients scheduled to undergo general anesthesia, 98 considered themselves to have been aware during previous surgery. The interview followed a structured protocol, including seven late symptoms (anxiety, chronic fear, nightmares, flashbacks, indifference, loneliness, and lack of confidence in future life). Three persons independently assessed the interviews to determine whether awareness had occurred. The result showed four cases were performed using regional anesthesia and another 29 were not considered as awareness by the assessors. Therefore, the final analyses included 46 patients. Twenty patients (43%) had experienced pain, and 30 patients (65%) described acute emotional reactions during the awareness episode. Fifteen patients (33%) had experienced late psychological symptoms. In six of those cases, the

symptoms lasted more than two months, and one patient had a diagnosis of post-traumatic stress disorder. Acute emotional reactions were significantly related to late psychological symptoms ($P < 0.05$).

Ghoneim, et al. (2009) revised awareness cases published between 1950 and 2005, and analyzed risk factors and causes. Two hundred and seventy-one cases of awareness were reported and these were compared with control patients from two large cohorts of surgical patients. The main cause of awareness was light anesthesia. Aware patients were more likely than controls to be younger, female, and undergoing obstetric or cardiac surgery. Thirty-eight percent of patients reported pain during the episode. Other complaints including hearing voices (66%), feeling helpless or anxious (34%), and inability to move (34%). Late psychological sequelae were noted by 22% of the patients.

Errando, et al. (2008) published a report of 3,921 patients who underwent non-cardiac surgery at a large Spanish institution. Thirty-nine cases of awareness were identified (1%) and higher incidences of awareness were reported in patients maintained with nitrous oxide (5%) or propofol (1.1%) than in patients maintained with volatile anesthetic agents (0.6%). Risk factors for awareness included cesarean section, omission of benzodiazepines and surgery at night. The researchers concluded that these resultsmay be due to a selection bias or use of techniques (such as nitrous oxide based anesthesia) that are associated with a high risk of awareness.

Xu, et al. (2009) conducted a prospective multi-centre study of 11,101 Chinese patients in whom general anesthesia was induced. The incidence of awareness was 0.41% and risk factors included higher-grade physical status according to ASA, previous anesthesia and total intravenous anesthesia. The authors suggested that the comparatively high incidence of awareness may be because the percentage of patients in China who undergo surgery under general anesthesia as opposed to those who have surgery under local or no anesthesia is much lower than in Western countries and may represent a high-risk group.

Paech, et al. (2008) reported a lower incidence of awareness in 1095 general anaesthetics obstetric patients than early published. The authors conducted a prospective cohort study in women undergoing Cesarean section under general anesthesia in Australia. They noted two cases of awareness; the authors attributed this comparatively low incidence of awareness to the increased obligation by anesthesiologists of the need for adequate doses of induction and maintenance agents during Cesarean section.

2.10 Studies of BIS monitoring

Several studies have been conducted in which the BIS monitor was used. BIS monitoring has been shown to lower the consumption of anesthesia drugs (Shafiq, et al. 2012) and improve recovery from anesthesia (Gan, et al. 1997, Song, et al. 1997). Reduction in the incidence of nausea and vomiting post-operatively was shown by Liu (2004). A somewhat positive

correlation between BIS and the prevention of post-operative delirium was found by Chan et al. (2013).

Chan, et al (2013) studied BIS monitoring in 921 elderly patients, 60 years or older. BIS monitoring was recorded for all study subjects, but anesthesiologists were not permitted to observe the monitor in the control group.. There was a significantly lower consumption of anesthetic agents (21 % reduction in propofol and 30 % reduction in volatile anesthetics) in the BIS group compared to the control group. The incidence of delirium was reduced from 24 % to 15% when BIS was used. Post-operative cognitive dysfunctions, which may result from long-lasting neurotoxicity of general anesthetics, appeared in both groups and there were no differences in the prevalence one week post-operation between the groups, but after three months the prevalence was lower in BIS group (10.2% vs 14.7%).

Caillouxb, et al, (2001) demonstrated that an anesthesiologist can control the level of consciousness of a patient undergoing surgery by appropriately dosing hypnotic drugs. The information provided by monitoring devices may be used to accomplish this task. One such monitor, Bispectral index (BIS), provides a dimensionless quantity derived from the electroencephalogram, which could quantify the level of awareness of a patient during surgery. This article discusses the use of machine learning techniques to implement a predictive model of the BIS based on the variation of the hypnotic drugs. Such a model developed from a database of recorded operations can aid real-time decision making during the course of an operation. In order to deal with inter-individual variability, the proposed

model takes into account patient physiology and reactions of the patient during the early phases of the operation. Two models of the Bispectral index are assessed and compared in this work: a linear predictor and a local learning predictor. These prediction models were software implemented and their accuracies were assessed by a computerized cross-validation study and were tested in real situations.

Croci, et al. (2012) reported that Bispectral index-guide anesthesia may reduce postoperative nausea and vomiting. The study aimed to investigate the effect of Bispectral index-guide anesthesia (BIGA) on the reduction of Postoperative Nausea and Vomiting (PONV). The authors conducted a prospective randomize control study which include 300 cases of gynecological laparoscopy surgery in women, age 22-68 (mean 43), ASA I-II, 150 with BIGA (A) and 150 no BIS used during anesthesia (B). The two groups were divided in three sub-groups: low, moderate and high risk of PONV according to a risk score. All patients were given a balanced general anesthesia (induction with propofol and maintenance with desflurane, no nitrous oxide). Prophylactic antiemetics were administered to patients with moderate (ondansetron) or high risk (ondansetron + dexamethasone),. No antiemetics were administered to the low risk group. The study result show the incidence of PONV in the group A (20%) was lower than in the group B (25%) in all three sub-group, especially in patients with moderate risk (18% (A) versus 24% (B)) and high risk (28% (A) versus 36% (B)) of PONV. The incidence of PONV in low risk patients was 12% (A) and 16% (B). The use of BIS monitoring reduced desflurane

consumption by 34.6% between group A and B ($p < 0.001$). Statistical analysis of data showed no significant difference in PONV between groups. These data confirm the importance of antiemetic drug treatment to prevent PONV. The data also showed an interesting reduction of PONV when anesthesia was performed under Bispectral index monitoring. BIGA is usually used to control the depth of anesthesia but may also have an effect on PONV. The study concluded that a BIGA, in combination with antiemetic therapy, could further reduce the incidence of PONV especially in patients with moderate or high risk. This difference is due to the reduction of volatile anesthetic used during anesthesia in group A with the use of BIGA.

Sebel, et al. (2004) conducted a study to determine the incidence of awareness during anesthesia. A multicenter, prospective, nonrandomized descriptive cohort study was conducted at seven academic medical centers in the United States. Patients scheduled for surgery under general anesthesia were interviewed in the postoperative recovery room and at least a week after anesthesia and surgery. The study included 19,575 patients. A total of 25 awareness cases were identified (0.13%). These occurred at a rate of 1–2 cases per 1000 patients at each site. Awareness was associated with increased ASA physical status (odds ratio, 2.41; 95% confidence interval, 1.04–5.60 for ASA status III–V compared with ASA status I–II). Age and sex did not influence the incidence of awareness. There were 46 additional cases (0.24%) of possible awareness and 1,183 cases (6.04%) of possible intra-operative dreaming. In summary, the incidence of awareness

during general anesthesia in the US was 0.13%. It occurred at a rate of 1–2 per 1000 patients interviewed at each site.

Myles, et al. (2004) conducted a study that aimed to determine whether BIS-guided anesthesia reduced the incidence of awareness during surgery in adults. The method was prospective, randomized, double-blind, multi-centre trial. Adult patients at high risk of awareness were randomly allocated to BIS-guided anesthesia or routine care. Patients were assessed by a blinded observer for awareness at 2-6 h, 24-36 h, and 30 days after surgery. An independent committee, blinded to group identity, assessed every report of awareness. The primary outcome measure was confirmed awareness under anesthesia at any time. The study included 2,463 eligible and consenting patients, 1,225 of whom were assigned to the BIS group and 1,238 to the routine care group. There were 2 reports of awareness in the BIS-guided group and 11 reports in the routine care group (p=0·22). BIS-guided anesthesia reduced the risk of awareness by 82% (95% CI 17–98%). The authors concluded that BIS-guided anesthesia reduces the risk of awareness in at-risk adult surgical patients undergoing relaxant general anesthesia.

Punjasawadwong, et al. (2014) conducted a systematic review of 36 randomized controlled trials comparing BIS with standard practice measures for titration of anesthetic agents. The results showed a significant effect of the BIS-guided anesthesia in reducing the risk of intra-operative awareness among surgical patients at high risk for awareness (7,761 participants). This effect was not seen in studies using end tidal anesthetic

gas (ETAG) monitoring as standard practice. Results showed that BIS-guided anesthesia eliminated the need for propofol by 1.32 mg/kg/hr (672 participants) and for volatile anesthetics (desflurane, Bispectral index for improving anesthetic delivery and postoperative recovery by 0.65 minimal alveolar concentration equivalents (MAC) in 985 participants. Regardless of the anesthetics used, BIS reduces the following recovery times: time for eye opening, response to verbal command , time to extubation, and time to orientation . BIS reduced the duration of postanesthesia care unit (PACU) stay but did not significantly lower the time to home readiness. Authors concluded that BIS-guided anesthesia can reduces the risk of intra-operative awareness in surgical patients at high risk for awareness in comparison to utilizing clinical signs as a guide for anesthetic depth. BIS-guided anesthesia and ETAG-guided anesthesia may be reciprocal in protection against intraoperative awareness. The authors also concluded that anesthesia regulated by BIS monitoring enhances anesthetic delivery and postoperative recovery from relatively deep anesthesia.

Avidan, et al. (2008) conducted a study to determine whether a BIS-based protocol is better than a end-tidal anesthetic gas (ETAG)-base protocol for decreasing anesthesia awareness in patients at high risk for this complication. The authors randomly assigned 2,000 patients to BIS-guided anesthesia or ETAG-guided anesthesia. Postoperatively, patients were assessed for anesthesia awareness at three intervals (0 to 24 hours, 24 to 72 hours, and 30 days after extubation). Results included assessment of 967 patients from the BIS group and 974 patients from ETAG group. Two cases

of anesthesia awareness occurred in each group. The BIS value was greater than 60 in one case of definite anesthesia awareness, and the ETAG concentrations were less than 0.7 MAC in three cases. For all patients, the mean (±SD) time-averaged ETAG concentration was 0.81±0.25 MAC in the BIS group and 0.82±0.23 MAC in the ETAG group (P=0.10); 95% CI for the difference between the BIS and ETAG groups, −0.04 to 0.01 MAC). The authors conclude that the results of this study do not support routine BIS monitoring as part of standard practice.

Mashour, et al. (2009) conducted a prospective, randomized, controlled trial comparing the Bispectral Index monitor to a non-electroencephalographic gauge of anesthetic depth. The sample size was 30,000 patients at both low and high risk for awareness. The authors developed a novel algorithm capable of real-time analysis of their electronic perioperative information system. In one arm of the study, anesthesia providers received an electronic page if the Bispectral Index value was >60. In the other arm of the study, anesthesia providers received a page if the age-adjusted minimum alveolar concentration was P <0.5 . The authors concluded that awareness during general anesthesia is a persistent problem and the role of the Bispectral Index monitor in its prevention remains unclear.

Mozafari , et al. (2014) conducted a study in Iran of 333 adult patients with ASA physical status I-III, aged between 18-65 years who underwent elective abdominal surgery under general anesthesia. The study participants were entered in a randomized double-blind placebo controlled trial.

Patients were randomly assigned to BIS monitoring (n=163) or routine monitoring (n=170). BIS values and hemodynamic parameters including systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), and SPO2 were noted before induction (control value), after intubation and laryngoscopy, at intubation, after incision, and every 15 minutes during the operation until extubation. The overall incidence of awareness in the BIS and routine monitoring groups was 5.5% and 4.1%, respectively. This difference was not significant. There were no significant differences between the BIS and routine monitoring groups in hemodynamic parameters before induction of anesthesia or at different time points after anesthesia induction. The authors concluded that BIS-guided administration of general anesthesia during abdominal surgeries may not be superior to routine monitoring in preventing awareness or controlling hemodynamic parameters.

Hadavi , et al. (2013) carried out a study in Iran on 60 parturient patients undergoing elective Cesarean section using a standardized anesthetic technique induced with thiopental and succinylcholine and maintenance with O2, N2O, and isoflurane. The researchers monitored hemodynamic parameters (electrocardiogram, heart rate, blood pressure, SpO2), end-tidal isoflurane concentration, BIS levels, and clinical signs of inadequate depth of anesthesia such as movement, sweating, lacrimation, coughing, and jerking. Recordings were taken at16 fixed time points during anesthesia. A median BIS of less than 70 (range: 42-68) was obtained at all time points during the surgery, with 20% of patients showing a BIS that did not dip

below 60 throughout the surgery. Hemodynamic parameters increased significantly in some patients, especially during laryngoscopy and intubation. No patient experienced recall or awareness. The authors concluded that general anesthetic technique seems inadequate in some events to reliably produce BIS values less than 60, which are associated with lower risk of awareness. Therefore, with concern to such desirable outcomes as good Apgar and clinical status in neonates, the authors recommend the application of this method (if supported by further studies) through larger dosages of anesthetic agents.

Chapter Three

Research Methodology

This chapter describes methods and procedures employed by the researcher including: determination of the methodology, study design, description of the sample, and preparation of the study tool, including validity and reliability measures. In addition the chapter includes a description of the procedure employed by the researcher in executing the study and a discussion of the statistical treatment used in data analysis.

Methodology

3.1 Study design

This study is a prospective, randomized, double-blind, controlled study. Patients were randomized to one of two groups: BISguided anesthesia and routine care. The patients were appraised by a blinded viewer for awareness at 24-36 hours. After surgery, a blinded separate panel unaware of group identity evaluated each awareness report.

3.2 Study population

The study group consisted of adult men (n=41) and women (n=18), above 18 years, undergoing various types of elective surgery under general anesthesia at An-Najah National University Hospital between September-December 2015.

3.3 Sampling of the study

The study sample consisted of (60) patients randomized to either:

Group (1), n=30 patients who had BIS-guided general anesthesia. Note, one patient withdrew from the study so Group (1) is n=29 patients.

Group (2) n=30 patient who had routine care under general anesthesia

It was determined that the minimal sample size for this study, to assure adequate power (80%) and to detect statistical significance ($p<0.05$), was 17 people in each of the two groups. But to increase the power of our study, we recruited 30 patients in each group.

3.4 Anesthesia protocol

- Functional anesthesia system was checked thoroughly (evaporators, infusion pumps, fresh gas flow and intravenous lines) have been verified to reduce the risk of intraoperative awareness.

- General anesthesia has three components: amnesia, analgesia and muscle relaxation. The anesthetist monitors the depth of anesthesia by administering three types of drugs: hypnotics, to cause and maintain unconsciousness; analgesics, for inhibiting pain; and muscle relaxants, to block the muscle reactions. The dosages of these drugs are titrated to meet the specific needs of each patient.

- Patients are premedication with midazolam (2mg) administered intervenously

- A standardized anesthetic technique applied: induction with fentanyl (2 mcg / kg / dose), propofol (2 mg / kg), and Norcuron rocuronium bromide (1 mg / kg) followed by maintenance therapy with O2, N2O and sevoflurane. ECG, heart rate, blood pressure, SpO2, end-tidal sevoflurane concentration, BIS, and clinical signs of lack of depth of anesthesia (movement, sweating, tearing, coughing, and jerk) is continuously controlled and recorded.

- Bispectral index (BIS) commercialized by (Covidien BIS loc 2 channels). is connected via electrodes to the patient's forehead and is a signal derived from the electro-encephalographic activity of the patient.

- Bispectral Index (BIS) commercialized by (covidien BIS loc 2 channel). is attached via electrodes to the patient’s forehead after preparation of the skin of the patient by cleaning the pan with the alcohol to provide good electrical contact and exhibit a signal that is derived from the electro-encephalographic activity of the patient.

- BIS value ranges from 0-100. A BIS value of 0 as EEC silences, while close to 100, the value of a fully awake adult. Values between 40 and 60 indicates an adequate level of anesthesia recommended by the manufacturer.

- BIS signal is near to 100 at the start of the operation when the patient is conscious and falls to about 50 after the induction stage when the patient loses consciousness.

- BIS value is checked in the 40-60 range by the end of the operation when the anesthetist stops the delivery of anesthetic and the patient wakes up.

- The BIS monitor allows the anesthesiologist to detect excessively high or low hypnosis and consequently to adapt the titration of the anesthetic agents to avoid unsafe states.

- Changes in anesthetic delivery led by the presence of clinical signs in relation to the BIS value. If the patient had hypertension or tachycardia and BIS value was> 60, was sevoflurane level increased. If BIS values were in the target range of 50-60, then fentanyl administered. If the BIS value <50 then sevoflurane was reduced and the patient is monitored for

lack of pain relief. In the control group , anesthetist could change anesthesia management, at its discretion, based on the patient's needs.

- BIS Monitoring started before anesthesia induction and during surgery. The monitoring was discontinued when patients achieved emissions from the operating room
- An end-tidal agent monitor was used.

3.5 Outcomes

3.5.1 Primary outcome measure

Intraoperative awareness

3.5.2 Secondary outcome measures

- Anesthetic consumption
- Recovery outcomes (time to extubation)
- Time to eye opening (either voluntary or in response to request
- Time to discharge from the PACU
- Intra-operative inhalation anesthetic medications consumption
- Intra-operative medications consumption
- Postoperative Nausea and vomiting (PONV)
- Pain

3.6 Questionnaire

Each study subject was interviewed by a blinded observer following surgery. The questionnaire included demographic information, including (gender, age, BMI, smoking, previous surgery, previous medications, and chronic diseases) (Appendix IV).

Interview questions (appendix II) about postoperative assessment of awareness were selected from questionnaires used in previous studies of awareness (**Hadavi, et al. 2013, Brice et al. 1970, Myles et al. 2004**).

3.7 Validity of the Interview tool

The validity of the interview tool was verified by a team five arbitrators (two anesthesiologists, two anesthetic nurses and one statistician) after all members of the team unanimously agreed on the questions.

3.8 Reliability of the Interview tool

The reliability of the interview tool was confirmed by determining the reliability coefficient using the Chronbach Alpha Equation. The reliability was equal or up to 0.07% which is considered acceptable.

3.9 Study measures

3.9.1 Variables of the study

Age, gender, smoking, ASA status, weight, height, BIS value, SBP, DBP, MAP, HR, and SPO2 were deliberated and registered before induction (control value), after intubation and laryngoscope for intubation, after incision, and every 5 minutes during the operation until the extubation (When the operation is complete and the adhesive bandage is applied to the surgical site, it was time for extubation that determined from that moment until the endotracheal tube was extubated), consumption of anesthetic agents, lacrimation, coughing, sweating, and movement were measured throughout the duration of anesthesia and surgery, and the time of discharge from PACU was recorded.

3.9.2 Randomization and blindness

Following signing of consent documents, patients were randomized to receive BIS-guided anesthesia (BIS group) or routine anesthesia care (routine care group). All other conditions of perioperative remained invariable between the two groups. In the BIS group, the responsible anesthesiologist had continuous access to BIS information. In the control group, anesthetist could change anesthesia management, at its discretion, based on the patient's needs.

Follow-up interviews were conducted by a blinded observer. Random assignment to study groups was achieved by envelopes, containing random

numbers previously prepared by a person who is not involved with any other part of the study.

3.9.3 Procedure

After receiving approval from the Institutional Review Board An-Najah National University and the achievement of written informed consent from all patients, 60 patients with American Society of Anesthesiologists [ASA] physical status I-III, anticipated for various types of elective surgery under general anesthesia were recruited in the study. After 3-5 minutes of preoxygenation in a 10-15 ° inclined position, anesthesia was calculated by 1.5µg / kg fentayl, 2-5mg / kg propofol and 1 mg / kg Norcuron. Anesthesia was maintained by O2, N2O and Sevoflurane (1-1.5%). ECG, BP, HR, SpO2, and BIS were monitored regularly all throug the surgical procedure. End-tidal seveflurane, N2O and CO2 concentration was measured under anesthesia. Patients received fentanyl (1 microgram / kg) intravenously if there were clinical signs suggestive of a lack of depth of anesthesia, including an increase of> 20% of pre-anesthetic values in HR and MAP, tearing, coughing, sweating, and movement. All data were registered by a person, who was not knowledgeable of anesthesia management protocol and technique. BIS, HR and BP were measured and documented at designated points during anesthesia: before induction; 30 seconds after laryngoscopy and intubation and continues to be registered every 5 minutes until extubation of the patient.

Sevoflurane and nitrous oxide were stopped upon the start and completion of skin closure, respectively. Reversal of muscle relaxation (by neostigmine and atropine) was administrated during skin closure.

Patients were inquired to open their eyes at one-minute intervals after extubation. The time period from the termination of the inhalational agents to eye opening was noted.

The time period from cessation of inhalational agents to eye opening was noted.

All patients were interviewed 24-36 h after surgery to determine awareness.

The primary endpoint was the confirmation of awareness, as defined by the patient's memory of intraoperative events, determined by interview.

Each member of the review committee which Composed of two anesthesiologists, three certified registered nurse anesthesia interviewed the results, the independent coded each report that "awareness" or "no awareness".

Accepted awareness was defined as a unanimous coding of “awareness” or two committee members coding as “awareness”.

The recovery time was measured from the completion of wound dressings and for most patients included eye opening and qualification for discharge.

3.10 Inclusion criteria for subjects in the study group

- 18 years or older
- Males & females
- Elective surgery of different types
- General anesthesia

3.11 Exclusion criteria for study group

- Use of beta-blockers: Patients on beta blockers that provide muscle relaxants during surgery, in association with beta-blockers may mask fast heart rate, physical movements, or hemodynamic changes (JCAHO 2004).
- Patients with traumatic brain injury, memory impairment, psychosis, known or suspected electroencephalograph abnormality (eg, epilepsy, previous brain resection, or scarring).
- Patients with a history of mental disease
- uncooperative patients
- Patients with language barrier problems
- Patients with history of awareness
- Patients with opium addiction
- Patients with neuromuscular disorders.

3.12 Statistical analysis

The statistical analyzes were performed by the SPSS software 21. A statistical power analysis was performed to determine the size of study

required to show that the BIS monitor reduces intraoperative awareness. We took 30 patiens for each group. Statistical measures calculated were:

1. Frequencies and percentages.
2. Mean and Standard Deviation.
3. Chronbach alpha coefficient.
4. Mann-Whitney Test of differences in all quantitative variables under study such as (SBP, DBP, MAP, SAO2 etc..) due to the group type (Routine Care group and BIS group).
5. Chi Square Test of Association between each categorical variable under study such as (age categories, surgical time categories and gender) and the group type (Routine Care group and BIS group).

3.13 Ethical consideration

The ethical principles followed are respectful, informed consent, charity, no harm done, truth and justice, explanation of research protocols to the patient, and the IRB. The study follows the World Medical Association Declaration of Helsinki Ethical Principles for Medical Research on humans (World Medical Association, 2013).

Prior to the commencement of data collection, approval for this study was obtained from the An-Najah University Institutional Review Board (IRB).

To mitigate bias and ensure the confidentiality of all study participants, identification numbers were assigned to each patient to avoid using any patient or provider information that would identify the patient/provider.

No hazards to participation were identified for this study. The researchers met with all patients undergoing surgery with general anaesthesia in the preoperative holding area on the day of the scheduled surgical procedure.

The researchers explained the purpose of the study, the participant's role in the study, privacy concerns, and the right to refuse participation. At that time, all patients who met the criteria enrolment invites to participate in the study.

Chapter Four

Results

4.1 Introduction

Fifty-nine patients were randomly assigned to BIS-steered anesthesia (n=30) or routine care group (RC) (n=29).

Table (1): Comparison of Demographic Variables and Clinical Characteristics between Study Groups (Routine Care and BIS).

Variable	Routine Care group N=29	BIS group N=30	P-value
Mean Age	41.11±18.892	43.34±16.363	0.571
Mean Weight	77.17±17.994	75.79±14.369	0.889
Mean Height	170.25±7.347	169.97±8.695	0.955
Patient Metabolic Index	26.62±4.70	26.14±4.00	0.690
Gender-male	20(69%)	21(70%)	0.931
Gender-female	9(31%)	9(30%)	
Previous surgery-Yes	18(64.3%)	18(62.1%)	0.862
Previous surgery-No	10(35.7%)	11(37.9%)	
Previous medication-Yes	6(22.2%)	5(17.2%)	0.639
Previous medication-No	21(77.8%)	24(82.8%)	
Smoking-Yes	11(37.9%)	15(51.7%)	0.291
Smoking-No	18(62.1%)	14(48.3%)	
Chronic diseases-Yes	11(37.9%)	10(34.5%)	0.785
Chronic diseases-No	18(62.1%)	19(65.5%)	

*Significant at 0.05 level. Data are Mean±SD with P-values derived from Mann-Whitney U test or Frequencies and Percentages (%) with P-values derived from Chi Square test.

Patient demographics and clinical characteristics for the two study groups are shown in **Table 1**. There are no significant differences between the two groups in all general characteristics of patients.

Table (2): Comparison of Induction Agent Levels between Study Groups (Routine Care and BIS).

Induction Agent	Routine Care group N=29	BIS group N=30	P-value
Propofol mg	230±59.938	474.07±711.3	0.235
Midazolam mg	1.17±0.408	1.5±1	0.648
Fentanyl (µg)	77.76±40.523	115.56±94.18	0.035*
Inspired concentration of the Sevoflurane	0.028±0.007 (0.011-0.04)	0.024±0.013 (0.0-0.07)	0.043*
Mean dose of i.v. anesthetic agent (mg)	221.07±56.197	260.67±243.678	0.936
Mean dose of inhaled anesthetic agents	0.029±0.008 (0.012-0.04)	0.025±0.009 (0.01-0.035)	0.023*
End-tidal sevoflurane concentration %	0.054±0.166 (0.008-0.9)	0.018±0.012 (0.006-0.06)	0.004*

*Significant at 0.05 level. Data are Mean±SD with P-values derived from Mann-Whitney U test or Frequencies and Percentages (%) with P-values derived from Chi Square test.

The table (2) above shows that there is a statistically significant difference in the inspired concentration of the anesthetic between the two groups under study. For the Routine Care group the mean value was 0.0282 which was reduced to 0.024%, for the BIS group, P-value was 0.043. The data also show a statistically significant difference in the mean dose of inhaled anesthetic agents between the two groups: For the Routine Care group the mean value was 0.029% which was reduced to 0.025%` for the BIS group, and the P-value was 0.023. There is statistically significant difference in the end-tidal sevoflurane concentration: the mean value was 0.054 for the Routine Care group and 0.018 for the BIS group, and the P-value was 0.004. There is statistically significant difference in sevoflurane dosage between the two groups: for the Routine Care group the mean value was 0.028 and 0.023 for BIS group with the P-value = 0.023.

There is a statistically significant difference in the fentanyl dosage between the two groups: for the BIS group the mean value was 115.56 which was reduced to 77.76 for the Routine Care group with the P-value = 0.035.

Table (3): Difference Between Intraoperative Physiological Variables between Study Groups (Routine Care and BIS).

Variable	Categories	Routine Care group N=29	BIS group N=30	P-value
Intraoperative Sweating	No	29(100%)	26(96.3%)	0.296
	Yes	0(0%)	1(3.7%)	
	Missing	0	3	
Intraoperative Lacrimation	No	24(85.7%)	25(89.3%)	0.686
	Yes	4(14.3%)	3(10.7%)	
	Missing	1	2	
Pupillary Dilatation	No	27(96.4%)	26(92.9%)	0.553
	Yes	1(3.6%)	2(7.1%)	
	Missing	1	2	
Intraoperative Coughing	No	28(96.6%)	29(100%)	0.313
	Yes	1(3.4%)	0(0%)	
	Missing	0	1	
Intraoperative Jerking	No	21(72.4%)	27(93.1%)	0.037*
	Yes	8(27.6%)	2(6.9%)	
	Missing	0	1	

*Significant at 0.05 level. Data are Mean±SD and (Minimum-Maximum) with P-values derived from Mann-Whitney U test or Frequencies and Percentages (%) with P-values derived from Chi Square test.

The table (3) above shows that there is statistically significant difference between the Group Type and the Intraoperative Jerking with the percentage of Intraoperative Jerking reduced from 27.6% in the Routine Care group to 6.9% in the BIS group with a P-Value of the Chi Square test of 0.037.

There are no statistically significant differences between the group types and all the other variables under study.

Table 4: Differences in Anesthesia Management Time Variables Between Study Group (Routine Care and BIS).

Variable	Routine Care group N=29	BIS group N=30	P-value
Tme of surgery(minutes)	73.8±85.8	116.4±106.2	0.194
Length of Procedure (minutes)	76.6±84.3	124.2±124.4	0.207
Time from cessation of inhalational agents to eye opening (minutes)	7.32±4.643	5.19±3.462	0.087
Time to response to commands (minutes)	10.03±5.335	8.11±4.516	0.205
Time to eye opening (either spontaneously or in response to command) (minutes)	10.81±5.955	8.24±4.833	0.086
Time to first movement response (minutes)	7.69±6.03	5.31±3.878	0.174
Time to phonation (minutes)	12.82±6.11	10.21±5.127	0.026*
Time to extubation (minutes)	8.64±4.775	7.25±4.106	0.278

The table (4) above shows that there is a statistically significant difference in time to phonation between the two study groups with the mean time to phonation for the Routine Care group equal to 12.82 minutes and the mean time for BIS group 10.21 minutes and the P-value of the Mann-Whitney test at 0.026.

There are no statistically significant differences between the two study groups in any of the remaining time measures under study.

Table (5): Differences in Nausea and Pain Between Study Groups (Routine Care group and BIS group).

Variable	categories	Routine Care group N=29	BIS group N=30	P-value
Nausea (yes/No)	No nausea	29(100%)	26(100%)	-----
	Missing	0	4	
Pain 0(no pain) 1-3(Mild) 4-6(Moderate) 7-8(Severe) 9(Very Severe) 10(Worse Possible)	No Pain	19(67.9%)	20(76.9%)	0.011*
	Mild	7(25%)	0(0%)	
	Moderate	2(7.1%)	6(23.1%)	
	Severe	0(0%)	0(0%)	
	Very Severe	0(0%)	0(0%)	
	Worse Possible	0(0%)	0(0%)	
	Missing	1	4	

*Significant at 0.05 level. Data are Mean±SD and (Minimum-Maximum) with P-values derived from Mann-Whitney U test or Frequencies and Percentages (%) with P-values derived from Chi Square test.

The table (5) above shows that there is a statistically significant differences association, at the significance level $\alpha < 0.05$, in perception of pain between study groups. 25% for the Routine Care group expressed mild levels of pain while 0% of the BIS group expressed mild pain : This happened because the BIS group had mild pain less than expected (count=0 and expected count=3.4), while the Routine Care group had mild pain more than expected (count=7 and expected count=3.6). On the other hand, 7.1% of the Routine Care group expressed moderate levels of pain, while 23.1% of the BIS group had moderate levels of pain.This happened because the BIS group had moderate pain more than expected (count=6 and expected

count=3.9),while the Routine Care group had mild pain less than expected (count=2 and expected count=4.1). The P-Value of Chi Square test is 0.011.

How we get the expected?

The chi square test is constructed by the difference between the observed counts and the expected counts, so it is important to mention the expected value for the cell in the cross tabulation when we get significant chi square value.

Table (6): Differences in Recovery time, Discharge Criteria Score, Time to Discharge from the PACU between Study Groups (Routine Care group and BIS group).

Variable	Routine Care group N=29 Mean±S.D	BIS group N=30 Mean±S.D	P-value
Recovery time (minutes)	11.64±5.09	9.95±4.261	0.210
Discharge Criteria Score Aldrets Score	9.72±0.75	9.7±1.67	0.185
Time to Discharge from the PACU (minutes)	12.38±4.989 (6-26)	9.23±3.819 (4-20)	0.007*

*Significant at 0.05 level. Data are Mean±SD and (Minimum-Maximum) with P-values derived from Mann-Whitney U test or Frequencies and Percentages (%) with P-values derived from Chi Square test.

The table (6) above shows that there is a statistically significant difference at the significance level $\alpha < 0.05$ in the time to discharge from the PACU between the two study groups: the mean time to discharge from the PACU was 12.38 minutes for the Routine Care group and 9.23 minutes for the BIS group, with a P-value 0.007.

There are no statistically significant differences in all the other variables under study.

Table (7): Differences of Anesthesia Management Parameters (SAT, Co2, HR, SBP, DBP, MAP and Pre and Post Operation Parameters) Between Study Groups (Routine Care and BIS).

Parameter	Routine Care group N=29	BIS group N=30	P-value
SAT (SPO2)%	98.52±1.01	98.7±1.35	0.249
end-tidal CO2 (mm Hg)	33.88±4.34	33.86±3.66	0.739
HR (beat /min)	78.77±12.37	77.25±13.27	0.544
SBP (mmhg)	112.64±19.13	116.91±21.82	0.458
DBP (mmhg)	69.9±16.15	70.2±13.39	0.779
MAP (mmhg)	83.38±14.79	84.87±14.86	0.514
Pre Operation HR (beat/min)	81.03±15.873	88.17±21.28	0.395
Pre Operation Systolic Blood Pressure (mmhg)	142.14±27.601	142.5±28.137	0.891
Pre Operation Diastolic Blood Pressure(mmhg)	87.28±20.32	86±16.233	0.976
Pre Operation O2 SAT%	98.48±2.011	99±1.857	0.330
Pre Operation RR (breath/min)	13.93±2.071	15.13±2.013	0.033*
Pre Operation TEMP(°C)	36.643±0.2026	36.663±0.2883	0.514
Post Operation HR (beat/min)	78.58±17.948	89.67±26.192	0.155
Post Operation Systolic Blood Pressure (mmhg)	132.79±25.518	135.62±20.812	0.665
Post Operation Diastolic Blood Pressure mmhg	86.53±17.36	84.62±16.963	0.776
Post Operation O2 SAT (%)	99.05±1.682	99.19±1.078	0.755
Post Operation RR (breath/min)	14.68±1.916	15±1.581	0.525
Post Operation TEMP (°C)	36.195±1.2782	36.455±0.4522	0.221

*Significant at 0.05 level. Data are Mean±SD and (Minimum-Maximum) with P-values derived from Mann-Whitney U test or Frequencies and Percentages (%) with P-values derived from Chi Square test.

The table (7) above shows that There is a statistically significant difference, at the significance level $\alpha < 0.05$, between the two study groups (BIS and Routine Care) in the Pre Operation RR. The Pre Operation RR per min for the BIS group had a mean value of 15.13, SD=2.013 and the

Pre Operation RR for the Routine Care group had a mean value of 13.93, SD=2.071 with the P-value 0.033. Values of Pre-Operative RR for both groups are within the normal range so there is no clinical importance to this difference. There are no statistically significant differences between the two groups (BIS group and Routine Care) in the remaining variables (SAT, CO2, HR, SBP, DBP, MAP and the remaining Pre and Post Operation Parameters).

Table (8): Difference in Anesthesia Management Parameters (SAT, CO2, HR, SBP, DBP and MAP) Across Time for Routine Care and BIS Study Groups

Parameters at Specific Time Points-Minutes	Routine Care group N=29	BIS group N=30	P-value
SAT_35 (%)	98.32±1.145	99.08±1.1	0.014*
SAT_40 %	98.21±1.285	98.96±1.186	0.030*
SAT_45 %	98.11±1.823	99.05±1.046	0.046*
SAT_50 %	98.32±1.293	99.1±1.513	0.010*
SBP_50 (mmHg)	109±28.08	128.45±25.482	0.016*
SBP_55 (mmHg)	103.75±20.722	122.25±27.34	0.028*
SBP_60 (mmHg)	100.08±28.268	126.29±32.031	0.034*
DBP_50 mmHg	61.18±15.593	76±15.922	0.008*
DBP_55 (mmHg)	62.33±15.656	72.68±16.62	0.039*
MAP_50 (mmHg)	77.56±17.494	92.57±19.836	0.012*

*Significant at 0.05 level. Data are Mean±SD and (Minimum-Maximum) with P-values derived from Mann-Whitney U test or Frequencies and Percentages (%) with P-values derived from Chi Square test.

The table (8) above shows that There are statistically significant differences between the BIS and Routine Care groups in SAT at the

following time points during operations: 35 min (Routine Care mean=98.32%,, BIS mean=99.08%), 40 min (Routine Care mean=98.21, BIS mean=98.96%), 45 min (Routine Care mean=98.11, BIS mean=99.05%), 50 min (Routine Care mean= 98.32, BIS mean=99.10), but this data has no clinical relevance because all values are within normal range. There are statistically significant differences between the two study groups in SBP during Operation at the following time points: 50 min (Routine Care mean=109 mmHg, BIS mean=128.45mmHg), 55 min (Routine Care mean=103.75mmHg, BIS mean=122.25mmHg), 60 min (Routine Care mean=100.08mmHg, BIS mean=126.29mmHg), but, again, this result has no clinical relevance since all values are in the normal range for both groups..

There are statistically significant differences between the two study groups (BIS and Routine Care) in DBP during Operation at the following time points: 50 min (Routine Care mean=61.18 mmHg, BIS mean=76), 55 min (Routine Care mean=62.33mmHg, BIS mean=72.68mmHg).

There are statistically significant differences between the two study groups (in MAP during Operation at the 90 minute time point (Routine Care mean=77.56mmHg, BIS mean=92.57mmHg). Finally, there were no statistically significant differences between the two study groups for all other variables and time points.

Table (9): Shows frequency, Percentages and the P-values of the Chi Square Test of Association between Awareness measurement and Gender, Surgical Time and Age Categories.

Variable/Category		Pure Awareness		P-value
		No	Yes	
Gender	Male(n=41)	39(95.1%)	2(4.9%)	0.578
	Female(n=18)	16(88.9%)	2(11.1%)	
Surgical Time	0-30 minutes(n=10)	10(100%)	0(0%)	0.675
	31-60 minutes(n=23)	20(87%)	3(13%)	
	61-90 minutes(n=10)	10(100%)	0(0%)	
	more than 90 minutes(n=16)	15(93.8%)	1(6.3%)	
Age Categories	less than 20(n=7)	5(71.4%)	2(28.6%)	0.235
	20-29(n=7)	7(100%)	0(0%)	
	30-39(n=14)	12(85.7%)	2(14.3%)	
	40-49(n=6)	6(100%)	0(0%)	
	50-59(n=14)	14(100%)	0(0%)	
	60-69(n=7)	7(100%)	0(0%)	
	70 or more(n=2)	2(100%)	0(0%)	

The table Above shows that there are no statistically significant association at the significance level $\alpha = 0.05$ between Awareness measurement and Gender, Surgical Time And Age Categories. (all P-Values > 0.05) (Table 9).

Table (10): Association between Awareness and Study Group (Routine Care and BIS).

Variable/Category		Group		P-value
		Routine Care (n=29) F(%)	BIS (n=30) F(%)	
Incidence of Awareness	No(n=55)	25(86.2%)	30(100%)	0.0.035
	Yes(n=4)	4(13.8%)	0(0%)	

Data are Frequencies and Percentages (%) with P-values derived from Chi Square test

The table Above shows that there is statistically significant difference at the significance level α =0.05 in awareness measurement between Routine Care group and BIS group (P-value=0.035<0.05). The Routine Care group(13.8%) have awareness more than BIS group(0%).

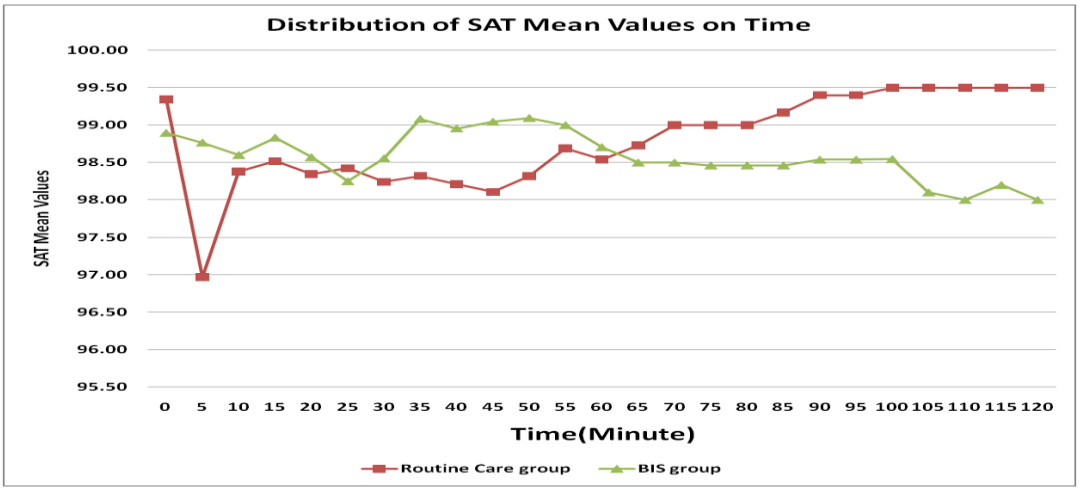

Figure 2. Distribution of SAT mean Values on Time

The plot above (Figure 1) shows a rise in SAT levels for the Routine Care Group over the SAT levels for the BIS groups after 60 minutes of

Operation Duration. The differences were significant only at the minutes (35, 40, 45, 50) in favor of BIS group. this result has no clinical relevance since all values are in the normal range for both groups.

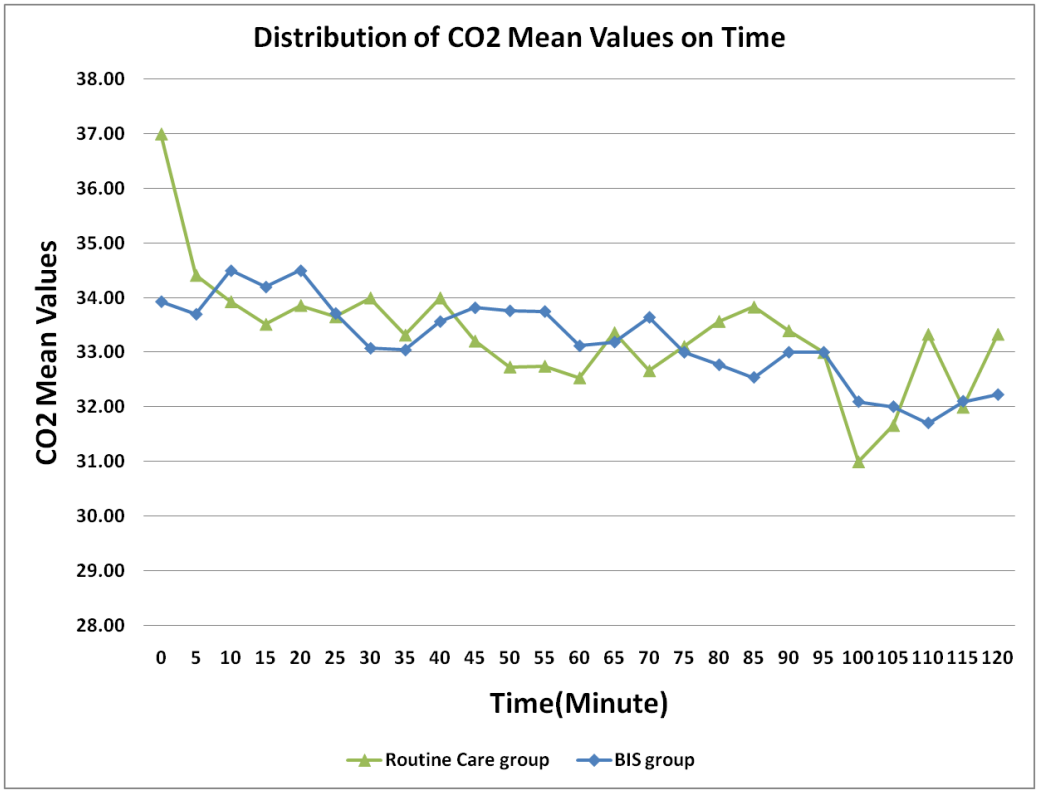

Figure 3. Distribution of CO2 Mean Values on Time

Figure 2 exhibits that CO2 parameters do not differ between the two study groups over duration of operation. There were no significant differences between each two corresponding points.

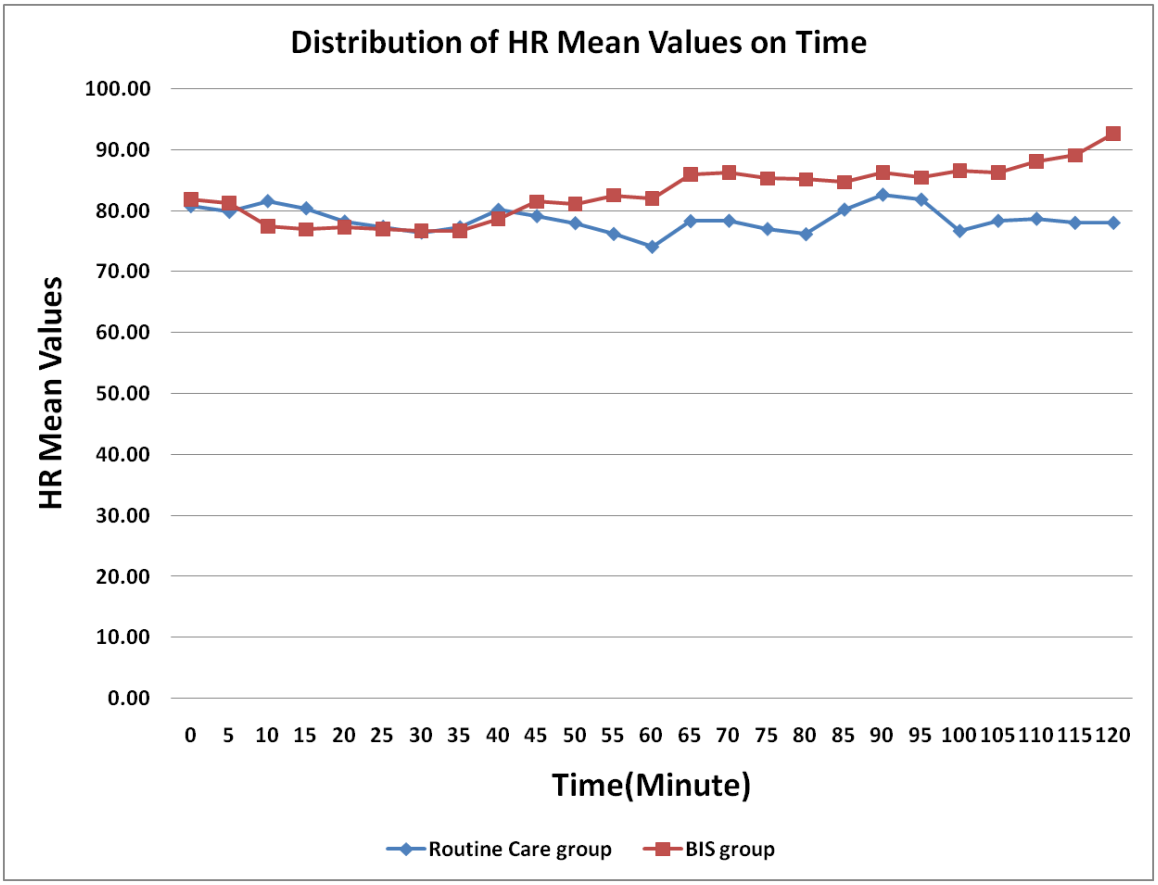

Figure 4. Distribution of HR Mean Values on Time

Figure 3 shows that HR levels do not differ between the study groups through the duration of the operation, except at the final time range (100 min and afterward) but it is not significant. There were no significant differences between each two corresponding points.

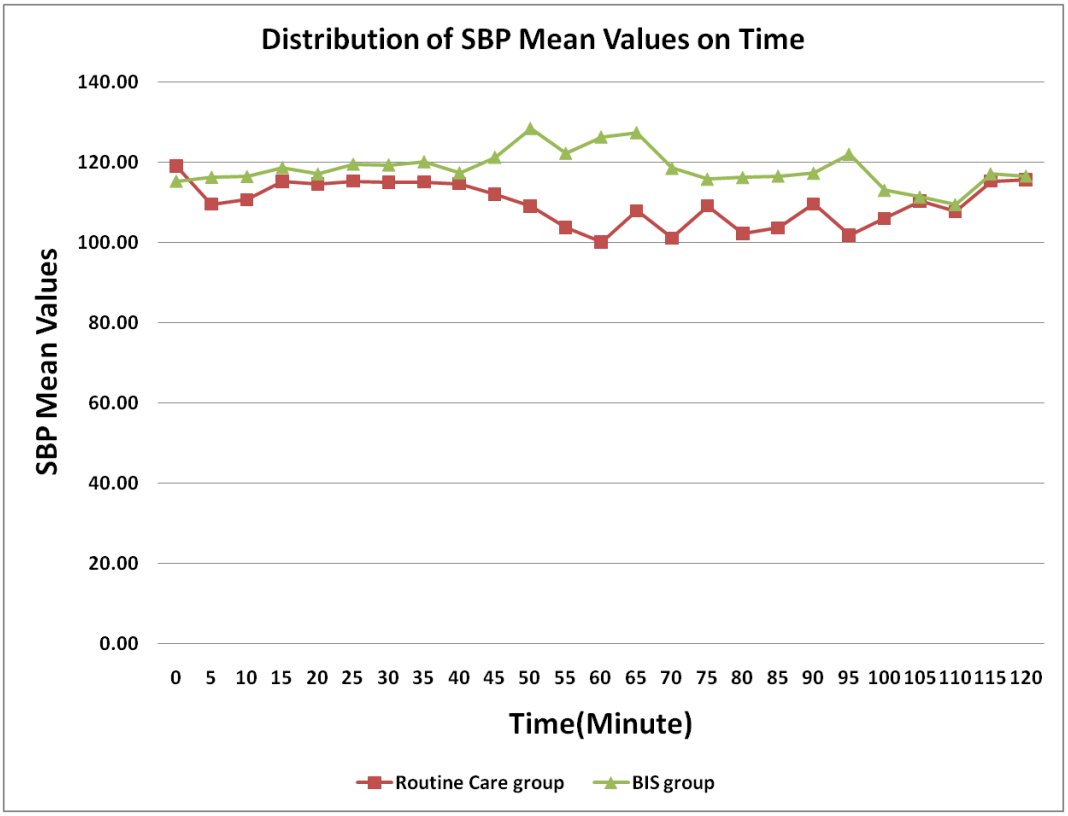

Figure 5. Distribution of SBP mean Values on Time

Figure 4 exhibits that the difference in SBP levels for the study groups does not differ through the duration of the operation. The differences were significant only at the minutes(50, 55, 60) in favor of BIS group. This result has no clinical relevance since all values are in the normal range for both groups.

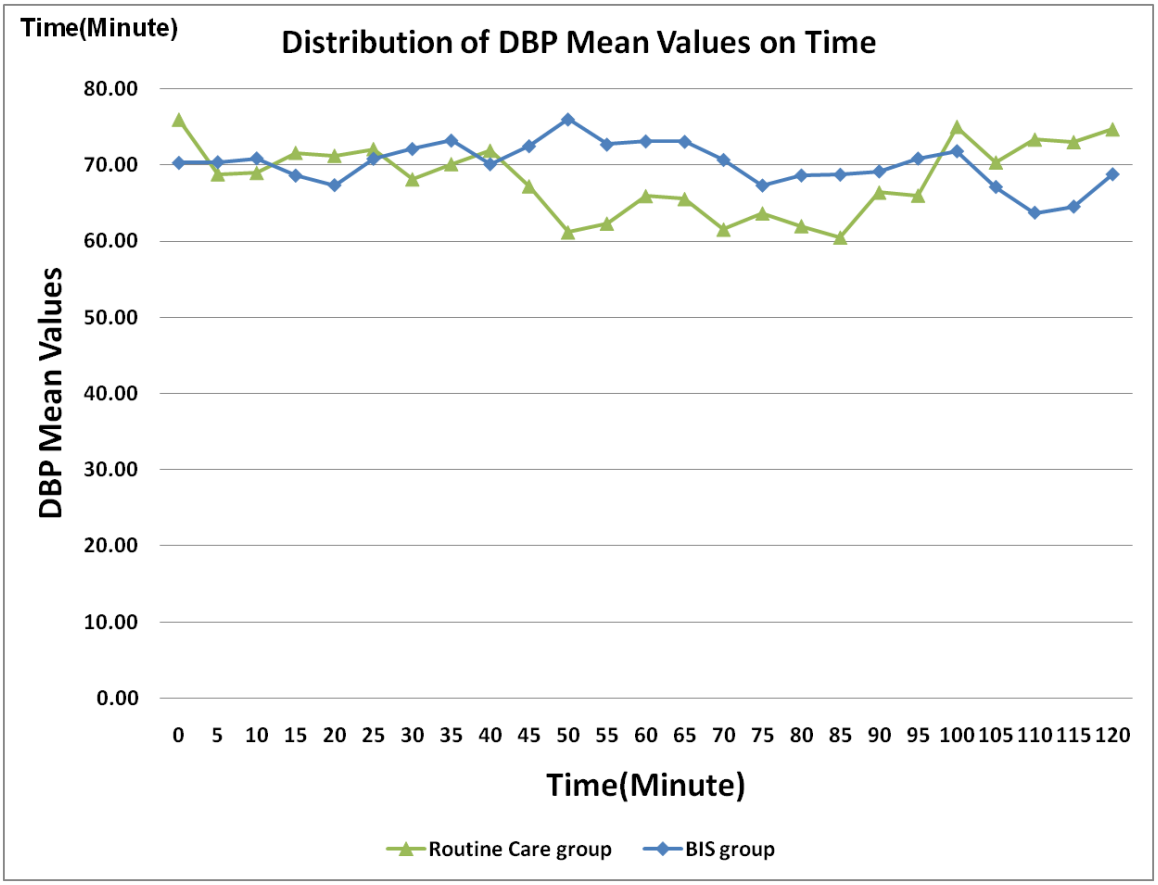

Figure 6. Distribution of DBP mean Values on Time

Figure 5 exhibits differences in DBP levels for the study groups, with the DBP of the BIS group higher than for the routine care group at the 50 to 55 minute time frame. The differences were significant only at the minutes(50, 55) in favor of BIS group. this result has no clinical relevance since all values are in the normal range for both groups.

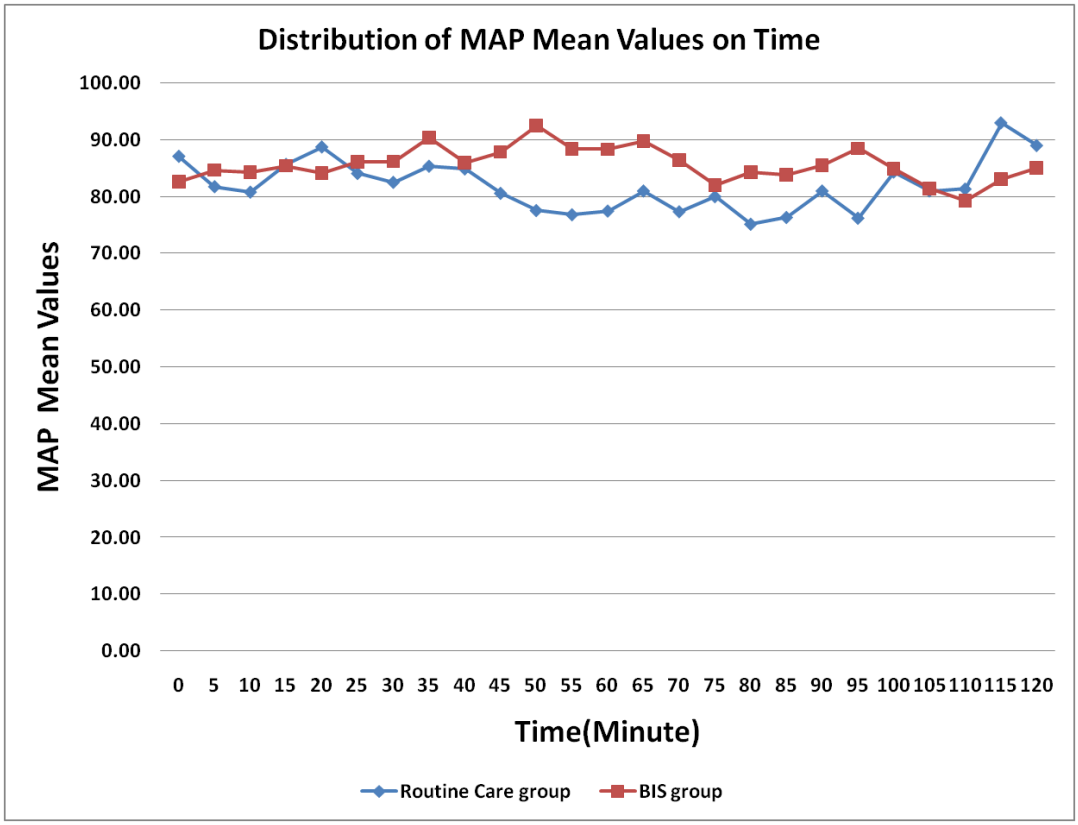

Figure 7. Distribution of MAP Mean Values on Time

Figure 6 shows differences in MAP for the study groups. The differences were significant only at the minute (50) in favor of BIS group. this result has no clinical relevance since all values are in the normal range for both groups.

Chapter Five

Discussion

This study was a prospective, randomized, double-blind, single-center study of 59 adult patients undergoing elective surgery under general anesthesia at An-Najah National University Hospital during September-December 2015. All study subjects were ASA physical status I-III, aged 18 to 72 years. Study participants were randomized to Bispectral Index (BIS steered anesthesia (n=30) or routine care group (RC) (n=29). At baseline, patients' demographic and clinical characteristics were comparable in the BIS and routine care groups. A BIS sensor was practiced to the forehead of patients and the value of the BIS index was recommended to be maintain between 40-60. BIS values, anesthetic agent consumption and hemodynamic parameters were recorded before anesthesia induction and during surgery every 5 minutes until extubation. Patients were interviewed by a blinded observer at 24-36 hours after surgery to determine experience of awareness. An independent committee, blinded to group identity, reviewed each report of awareness. The study aims to evaluate the clinical impact of BIS monitoring on perioperative parameters: hemodynamic variables, drug consumption, recovery times, end-tidal volatile anesthetic agents concentration and incidences of awareness.

BIS-guided anesthesia can reduce the risk of intra-operative awareness

We have found that BIS-guided anesthesia can reduce the risk of intra-operative awareness in surgical patients. We observed a statistically significant difference in occurrence of awareness between patients undergoing routine care during surgery (4 out of 29, 13.8%) and patients monitored by a BIS device during surgery (0 out of 30, 0%) (P=0.035). BIS-guided anesthesia decreased awareness by 13.8% (95% CI (1.3%-26.4%). These results are in agreement with previous findings of Ekman, et al. (2004) and Myles, et al. (2004

Our results are also in line with a systematic review conducted by Punjasawadwong study which provides sufficient evidence to support the use of BIS-monitoring to guide anesthesia administration and to prevent intr-aoperative awareness (Punjasawadwong, et al. 2014).

Our results confirmed by the findings of Sandin, et al. who reported a reduced risk of awareness of 13% over a control group when BIS monitoring was used during general anesthesia (Sandin et al. 2000). Our results are also in line with the study of Ekman, et al. (2004) who showed a 77% reduction in incidence of awareness after BIS monitoring. The results of this study are in accordance with the B-Aware trial, a multicenter, double-blind, randomized trial that evaluated the effectiveness of BIS monitoring in reducing awareness (Myles et al, 2004). This study reported an awareness risk reduction of 82% when BIS monitoring was used (95% CI: 17-98%), P=0.022.

Two different large, prospective trials reported an approximate 80% reduction in incidence of awareness after general anesthesia when BIS monitoring was used in comparison to routine monitoring (Ekman et al. 2004, Myles et al. 2004).

Results of the current study do not agree with the study of Mozafari, et al. (2014) who showed no evidence that BIS monitoring reduced awareness in patients undergoing abdominal surgery under general anesthesia compared to patients monitored by routine anesthesia administration protocols.

Avidan et al. (2008) compared a BIS-based anesthesia administration protocol and a protocol based on measurement of end tidal anesthetic gas (ETA) and investigated reduction of anesthesia consciousness. They found that anesthesia consciousness was similar between both groups.

Authors of the current study suggest that examining the anesthetic technique is important to understand the cause of awareness during anesthesia. Patients in the routine care group were given a smaller amount of propofol that produces hypnosis, and a smaller amount of fentanyl to relieve pain and suppress motion than patients in the BIS group. This may be the cause of the patients in the routine care group having awareness but not in the BIS group in the current study. This suggests that the patient can be exposed to light anesthesia. When anesthesia is too light, it can lead to recall events or conversations that take place in the operating room. The cause is not clear. On the other hand, monitoring the depth of anesthesia

using BIS should prevent intra-operative awareness and contribute to a precise dose of anesthetic.

Inhalational anesthetic agent consumption

The depth of anesthesia is measured by clinical parameters during anesthesia (for example, blood pressure, heart rate, or drug concentrations). These parameters become unreliable for measuring depth of anesthesia over the term of titration of anesthetic agents (Weber F, et al. 2005). Monitoring of inhalation anesthetic concentration by observing minimum alveolar concentration is part of routine anesthesia practice. It provides a method for monitoring the continuous brain concentration of volatile anesthetics. The BIS Index is a numerically treated, clinically validated EEG parameter that measures the effects of anesthesia and sedation on the brain (Bauer M, et al., 2004). According to the manufacturer of the BIS, this monitoring function provides a vital tool that allows clinicians to deliver anesthesia appropriate to a patient’s needs, and to assess and react appropriately to a patient's clinical condition during surgery. Over all, it can be helpful to maintain sufficient depth of anesthesia.

Our study showed a statistically significant reduction in the mean dose of inhaled anesthetics when using BIS monitoring as compared with routine care and anesthesia monitoring protocols. We also showed a statistically significant reduction in end-tidal sevoflurane concentration when using BIS monitoring as compared with routine care and anesthesia monitoring protocols. Our results are in agreement with studies by

Punjasawadwong, et al. (2014) who showed that BIS-guided anesthesia can significantly reduce anesthetic consumption and with and with Ibraheem et al. (2013) study who showed that The use of BIS monitoring was effective in reducing intraoperative desflurane requirements in patients undergoing laparoscopic sleeve gastrectomy.

Anesthetics drugs consumption

Our results showed a significant reduction in fentanyl dose when using BIS monitoring as compared with routine care and anesthesia monitoring protocols. These results were not consistent with other studies (Kreuer, et al., 2003; Leslie et al., 1995, Gan et al., 1997, Song et al. 1997).

Akcali, et al (2008) showed that consumption of propofol during induction was significantly lower when using BIS monitoring as compared with routine care during general anesthesia. Our results are not consistent with the study of Akcali, et al. Our data show that the consumption of propofol for induction does not differ significantly between BIS monitoring and routine care. However, we observed that patients in the BIS group consumed more propofol at induction than patients in routine care group (Table 2).

Driessen et al (1999) studied the application of a balanced anesthesia (propofol, alfentanil, and N2O) under BIS monitoring and routine care and found that propofol consumption was lower in the BIS group compared to routine group. Yili-Hankala, et al. (1999) compared propofol and sevoflurane under BIS and routine care protocols and found less

consumption of both propofol and sevoflurane in the BIS monitored group. These studies show the BIS monitoring is helpful for lowering the consumption of propofol during anesthesia. Friedberg et al. (1999), found that Bispectral (BIS) index monitoring decreased propofol consumption by 20% as compared to routine care.

Our results show that increasing the consumption of propofol, fentanyl and midazolam in the BIS group, this result is not in consistent with the study by Munoz Garcia J, et al. (2009) which mentions that BIS monitoring allows for reduced consumption of propofol, fentanyl and midazolam.

It is obvious that patients in the routine care group have been given a lesser amount of propofol and lesser amount of fentanyl than patients in the BIS Group. This has led to performing light anesthesia and this may be the cause of the patients in the routine care group having had more awareness than the BIS group in the current study.

Somatic response and clinical signs of awareness

Loss of somatic response due to painful stimuli is defined as no purposeful movement (twisting or jerking of the head, twitching or grimacing). In our study, we found no significant differences in somatic responses of sweating, tearing, pupil dilation and coughing between BIS monitored and routine care patients. We did note a significant reduction in intra-operational jerking between the BIS monitored and routine care patients.

That is, BIS is highly useful to prevent painful stimuli and maintain complete loss of somatic response to a nociceptive stimulus.

Time to extubation

Results of this study show no significant difference in time to extubation between the BIS monitored and routine care groups. This observation is not consistent with previous studies that showed that BIS monitoring is associated with reduced time to extubation. Akcali, et al. (2008), showed that time to extubation was significantly shorter under BIS monitoring than under routine care. Similar results were found by the following studies (Boztug, et al., 2006, Burrow, et al 2001, Gan et al., 1997, Yili-Hankala, et al., 1999. and Recart, et al. 2003).

The recovery time

In a systematic study review of Punjasawadwong, et al. (2014) showed that regardless of the anesthetic used BIS-guided anesthesia reduced all components of early recovery times, which is the time to open eyes, in response to the voice command, extubation and orientation. This information will help anesthesia providers to the tail doses of anesthetics at the end of the operation to the optimum light levels of anesthesia using BIS, and to facilitate recovery from anesthesia. In our study, we have been able to reduce time to eye opening, extubation time by BIS-guided anesthesia but the differences were not significant except we can significantly reduce the time of phonation Table (4). We do not agree with the study conducted by Kruerer et al. (2003) which found that the time to

open your eyes, extubation and arrival Post Anesthetic Care Unit (PACU) significantly reduced by using the BIS monitors. But the BIS monitoring had little effect on the time needed to recover from anesthesia, measured by eye opening (Sandin et al 2009, Myles et al. 2004)

Our study showed no significant difference in recovery time between the BIS monitored and routine care groups. These results are consistent with those shown by (Loveman, et al., 2001) who studied controlled infusion of propofol and remifentanil under BIS monitoring in neurosurgery patients and found that the BIS monitoring did not impact recovery time. In contrast, our results are not consistent with those of Dagtekin, et al., (2007) who reported that BIS monitoring facilitates stable hemodynamics and provides excellent recovery times for neuro-surgergical patients under Total Intravenous Anesthesia (TIVA). The authors propose a limitation of the current study is the total number of participants 59, and most studies of the BIS is performed with a larger number of participants. There may be a small sample size has affected the findings.

Time to discharge from PACU and Postoperative symptoms

We found a significant reduction in time to discharge from the PACU for BIS monitored patients as compared to patients in the routine care group. This result is consistent with the results from Punjasawadwong, et al. (2007), who concluded that the BIS monitoring reduced recovery times as measured by time to open eyes, response to verbal command time

to extubation, and orientation. They also showed that BIS monitoring was associated with shortened duration in the PACU.

Gan, et al. (1997) and Song, et al. (1999) suggest that cerebral monitoring can be useful to improve the titration of the anesthetic, which in turn leads to a faster recovery from anesthesia. Previously mentioned studies by Drover, et al.,(2002) and Recart, et al. (2003) did not find significant differences in length of stay or recovery time between BIS monitored and routine care patients.

Pavlin (1998) showed no impact of BIS-guided anesthesia in time to home readiness after ambulatory surgery despite a decline in PACU stay. They report that factors other than those related to anesthesia or surgery may have affected time of dismissal after ambulatory surgery. These included fatigue, nausea and vomiting, pain, lack of immediate access to an escort

Of note, in our study, the mild level of pain (25%) in the RC group as compared with 0% for the BIS group may be associated with the lower dose of fentanyl used for pain relief in the RC group as compared to the BIS Group. The authors suggest that it is possible that pain was a risk factor that led to the patients in the RC group taking longer to be released from the PACU than those in the BIS group. To compare the results of this study with previous studies of nausea, in the current study, four patients in the BIS group complained of nausea after surgery and 0 patients complained of nausea in the RC group. This result is not consistent with

results from Croci et al., which showed that the Bispectral Index-guided anesthesia can reduce postoperative nausea and vomiting (Croci et al. 2012) Of note is that the nausea had no effect on the time of discharge of patients in the BIS group from the PACU.

Hemodynamic parameters

This study showed significant differences in SBP, DBP and MAP at different points of operation between the BIS monitored group and the routine care group (Table 7). Our results confirm the findings from Mozafari, et al (2014) who found that changes in hemodynamic parameters were not dependent on the type of monitoring technology during abdominal surgery. Our results also agree with Payne et al.(2009) who reported that the hemodynamic responses during surgery do not decrease with BIS monitoring. The authors suggest that significant differences in SBP, DBP and MAP at different points of operation between the BIS and routine care group were not clinically relevant.

Awareness and gender, surgical time and age

This study showed no statistically significant association between awareness measurement and gender, surgical time and age. These results are in line with Sebel et al. (2004) who showed that age and gender did not affect the incidence of awareness. In the contrary, a study of Katoh et al. (2000) found that age strongly affected BIS points. At higher values of BIS, elderly subjects had higher probabilities of response compared to younger patients. Conversely, at lower values of BIS, elderly patients had a

lower probability of response . However, our findings are not consistent with those found by Ghoneim, et al. (2009) who reported that conscious patients were likely to be younger and women.. The authors proposed that, the limitation of the current study with a small sample size that contains different types of surgery that failed to detect the relationship between age, sex and time of surgery with awareness. Further research is needed with a larger sample size that includes the general population of surgical patients undergoing various types of surgery during general anesthesia.

Conclusion

BIS-guided anesthesia (BIS kept at 40-60) reduced the risk of awareness compared to routine care. The main reason for awareness of the RC group can considered a light general anesthetic. In addition, BIS monitoring reduces the usage of volatile anesthesia consumption and the time of discharge from the Post Anesthetic Care Unit.

Implications of BIS Monitoring for Anesthesia Nurses

Use of BIS monitoring is not very popular in a larger number of anesthesia departments (AD) in our country, even though the majority of anesthesiologists and anesthesia nurses working in AD are aware of the availability and function of BIS monitors. It is important that knowledge about improved anesthesia management be moved into the AD setting. BIS monitoring boosts the quality of patient care and should be an element of the standardized clinical practice in operating room settings

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Appendix I

The modified Aldrete scoring system for determining when patients are ready for discharge from the postanesthesia care unit (PACU).

Discharge Criteria Score	
Activity	
Able to move four extremities voluntarily or on command	2
Able to move two extremities voluntarily or on command	1
Able to move zero extremities voluntarily or on command	0
Respiration	
Able to deep breath and cough freely	2
Dyspnea, shallow or limited breathing	1
Apneic	0
Circulation	
Blood pressure +/ 20 mm of preanesthetic level	2
Blood pressure +/ 20 – 50 mm preanesthesia level	1
Blood pressure +/ 50 mm of preanesthesia level	0
Consciousness	
Fully awake	2
Arousable on calling	1
Not responding	0
O2 saturation	
Able to maintain O2 saturation > 92% on room air	2
Needs O2 inhalation to maintain O2 saturation >90%	1
O2 saturation < 90% even with O2 supplementation	0

A score of 9 was required for discharge from the PACU. From Aldrete JA. The post anesthesia recovery score revisited [letter]. J Clin Anesth 1995; with permission.

Appendix II-Interview Questions

Interview Question
Q1) Do you dream or have any other experiences while you were sleeping?
Q2) What was the worst thing about your surgery?
Q3) What was the next worst?
Q4) Do you remember anything in between?(before you went to sleep-l when you woke up)
Q5) What was the most unpleasant thing you remember from your operation and anesthesia?
Q6) Could you alert anyone during surgery?
Q7) Did you have any recall while surgery was being done?
Q8) Were you feeling surgical instruments or dressing application?
Q9) Were you hearing vague sounds?
Q10) Have you felt inability to move and feelings such as helplessness, sensation of weakness?

Appendix III. IRB

An - Najah
National University
Faculty of Medicine & Health Sciences
Department of Graduate Studies

بسم الله الرحمن الرحيم

جامعة النجاح
الوطنية
كلية الطب وعلوم الصحة
مركز الدراسات العليا

IRB Approval letter

Study title:
The clinical effectiveness of the Bispectral Index (BIS) to reduce the risk of awareness for elective surgical patients undergoing general anesthesia in Nablus district, A prospective, randomized, controlled study

Submitted by:
Tasneem Tarayrah

Date Reviewed:
Mar 18,2015

Date approved:
April 7, 2015

Your study titled: "The clinical effectiveness of the Bispectral Index (BIS) to reduce the risk of awareness for elective surgical patients undergoing general anesthesia in Nablus district, A prospective, randomized, controlled study" with archived number 25/Mar/2015 Was reviewed by An-Najah National University IRB committee & approved on April 7, 2015

Hasan Fitian , MD

IRB Committee Chairman
An-Najah National University

IRB

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Appendix IV. University Hospital Approval

An- Najah
National University
Faculty of Medicine & Health Sciences
Department of Nursing

بسم الله الرحمن الرحيم

جامعة النجاح الوطنية
كلية الطب وعلوم الصحة
دائرة التمريض

التاريخ: ١٣-٠٤-٢٠١٥

حضرة البروفيسور سليم الحج يحيى/ مدير مستشفى النجاح الوطني الجامعي المحترم ، ،

الموضوع: تسهيل مهمة الطالبة تسنيم طرايره

تحية طيبة وبعد،

تهديكم دائرة التمريض والقبالة في كلية الطب وعلوم الصحه/ جامعة النجاح الوطنية أجمل التحيات ونشكر لكم حسن تعاونكم المستمر معنا، أرجو من حضرتكم التكرم بالموافقه للطالبه تسنيم طرايره باجراء الدراسة البحثيه حيث أنها تدرس ماجستير تمريض التخدير وكمتطلب للتخرج يجب ان تنهي رسالة الماجستير تحت عنوان:

The clinical effectiveness of the Bispectral Index (BIS) to reduce the risk of awareness for elective surgical patients undergoing general anaesthesia in Nablus district, A prospective, randomized, controlled study.

لذا أرجو التكرم بالموافقه للطالبه والايعاز إلى رئيس قسم التخدير الدكتور وائل صدقة بالسماح للطالبه باجراء دراستها حيث أن المشرف الاكلينيكي على الدراسة الدكتور عبد الباسط نزال والدكتورة عائدة القيسي كمشرف رئيسي.

- مرفق طيه IRB

وتفضلو بقبول وافر الاحترام والتقدير ، ،

مديرة دائرة التمريض والقبالة

منسقة برنامج ماجستير تمريض التخدير

د. عائدة القيسي

مديرة دائرة التمريض والقبالة
في كلية الطب وعلوم الصحة
د. عائدة أبو السعود القيسي

جامعة النجاح الوطنية
كلية الطب وعلوم الصحة
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Appendix V

نموذج موافقة في المشاركة في دراسة بحثية

الفعالية السريرية لمؤشر ثنائي الطيف bispectral index (BIS) في تقليل خطر الصحو عند المرضى المعرضين لتخدير كلي في العمليات الجراحية الاختيارية في محافظة نابلس.

دراسة مستقبلية، عشوائية، عمياء، ومنضبطة.

سيطلب منك االمشاركة في دراسة بحثية. اسمي تسنيم الطرايرة. انا حاليا خريجة بدرجة الماجستير في تمريض التخدير في جامعة النجاح الوطنية، وانا الباحثة المسؤولة في هذه الدراسة، تحت اشراف د. عايدة القيسي ود. عبد الباسط نزال .

الهدف من هذه الدراسة :

استخدام مؤشر ثنائي الطيف (bispectral index) لمعايرة التخدير الكلي الذي سيسمح باستخدام عدد اقل من المواد التخديرية، تقليل المضاعفات الجانبية كالوعي اثناء العملية وتذكرها، والنهوض بعد العملية بشكل اسرع وافضل .

ماذا سيحدث اذا شاركت في هذه الدراسة؟

مساهمتك في هذا المشروع ستسمح لنا بوضع لاصق حساس على جبهتك. سيبقى على الجبهة طوال العملية الجراحية وسيزال بعد انتهائها فورا. هذا اللاصق الحساس سيكون موصولا بمؤشر ثنائي القطب الذي سيعطي قراءات تسمح بقياس درجة التنويم. هذا المؤشر مستخدم عالميا في NNUH ودول اخرى للمساعدة في تقييم عمق التخدير خلال العملية الجراحية .

الباحث المسؤول سيقوم بتسجيل معلومات طبية من سجلك الطبي، وهذه المعلومات ستضم: العلامات الحيوية (ضغط الدم، ضربات القلب)، استخدام الاكسجين ودرجة اشباعه (كمية الاكسجين في الدم)، الادوية والمواد التخديرية التي استخدمت في العملية الجراحية. ومعلومات اساسية كالعمر، الوزن، الجنس، الحالة اصحية العامة، والعمليات الجراحية السابقة .

ما هي مدة الدراسة؟

الملصق الحساس ستتم ازالته بعد انتهاء العملية الجراحية فورا وهذا سينهي اشتراكك في الدراسة.

ما هي المخاطر والفوائد من اشتراكي في الدراسة؟

المؤشر ثنائي الطيف سيسمح للمخدر بضبط كمية المواد التخديرية اللازمة للمريض والذي بدوره سيخرج المريض من التخدير بسرعة فور انتهاء العملية الجراحية. استخدام مؤشر ثنائي القطب سيسمح بتقليل وعي المريض للعملية الجراحية اثناءها.

ماذا لو غيرت رأيي بخصوص اشتراكي في الدراسة؟

مشاركتك في هذه الدراسة تطوعية. قد تختار ان تكون جزءا منها او لا تكون. وتستطيع الانسحاب متى شئت بغض النظر عن القرار الذي اتخذته لن يكون هناك مساءلة ولن تخسر فائدتك المرجوة من العملية. الانسحاب من الدراسة لن يؤثر على الرعاية الطبية المقدمة لك.

Appendix VI

Data collection sheet

Evaluation of sedation level using Bispectral Index

Student: Tasneem W Tarayrah

Supervisor: Dr. Aidah Abu Elsoud Alkaissi

Gender ◯ Male ◯ Female

Age: ……..

Type Of surgery: …….

Wight: ……..

Height:…….

Previous surgery: ◯ Yes : ……. ◯ No

Previous medications: ◯ Yes : ……. ◯ No ◯

Smoking Yes :…….. ◯ No

Chronic diseases: …….. ◯ No

BIS=bispectral index, EMG=electromyography, SQI=signal quality index, Sat=oxygen saturation, L/m=Liters per minute flow of oxygen, CO2=carbon dioxide's presence or absence, A/w=airway, Bolus=presence or absence of propofol bolus, HR=heart rate, SBP=systolic blood pressure, DBP=diastolic blood pressure, MAP=mean arterial pressure.
*L/m & Del iv: will be recorded at baseline and when any intraoperative changes from baseline occur *Sat: will be recorded at baseline, every 5 minutes.

	BIS	HR	BP	O2 SAT	RR	TEMP	TIME
Pre Op							
Post Op							

Min	0	5	10	15	20	25	30	35	40	45	50	55	60	65	70	75	80	85	90	95	100	105	110	115	120
BIS																									
Sat																									
Co2																									
Bolus																									
HR																									
SBP																									
DBP																									
MAP																									

A/W: C=chin Ieft, J=jaw thrust, B=combo of chin lift & jaw thrust, N=nasopharyngeal O=oroplaryngeal, M=mask ventilation, L=LMA placement, ETT=endotracheal tube placement
Deliv: O2 Delivery): NC=nasal cannula, FM=face mask, V=venturi mask, NRB=non-rebreather, M=mask ventilation, L=LMA, ETT=endotracheal tube
Time 0=when first BP is complete

The inspired concentration of the anesthetic	
the anesthetic time is recorded	
a mean dose of i.v. anesthetic agents is calculated Propofol	
a mean dose of inhaled anesthetic agents is calculated	
end-tidal sevoflurane concentration	
time of surgery	
Sweating intraoperative	
Lacrimation intraoperative	
pupillary dilatation	
Coughing intraoperative	
Jerking intraoperative	
The time period from cessation of inhalational agents to eye opening was noted.	
Time to response to commands	
Time to eye opening (either spontaneously or in response to command)	
Time to first movement response	
Time to phonation	
time to extubation	

Nausea (0-6 scale) No nausea, mild, moderate, severe, very severe, intolerable	
Vomiting (frequency)	
Pain (0-10) 0= no pain,10= intolerable pain)	
Time to discharge from the PACU.	

Postop Diagnosis: ……

Length of Procedure (mins): ……..

• Total drug dosages: ❑ Propofol:……..

❑ Midazolam: ……..

❑ Fentanyl: ……

❑ Sevoflurane: ……

❑ Other:……

Recovery time: ……

Appendix VIII

ASA physical status classification system for assessing a patient before surgery .

- **Normal healthy patient .**
- **Patient with mild systemic disease .**
- **Patient with severe systemic disease.**
- **Patient with severe systemic that is a constant threat to life .**
- **Moribund patient who is not expected to survive without the operation .**
- **Patient declared brain dead whose organs are to be harvested for donor purposes**

جامعة النجاح الوطنية

كلية الدراسات العليا

الفعالية السريرية لمؤشر رصد عمق التخدير Bispectral Index (BIS) للتقليل من حالة الوعي أثناء خضوع المرضى لمختلف العمليات الجراحية الاختيارية تحت تأثير المخدر العام – دراسة محتملة عشوائية – مزدوجة التعمية – ومراقبة

إعداد

تسنيم طرايرة

إشراف

د.عائدة القيسي

قدمت هذه الأطروحة استكمالا لمتطلبات الحصول على درجة الماجستير في تمريض التخدير، بكلية الدراسات العليا في جامعة النجاح الوطنية، في نابلس – فلسطين.

2017

الفعالية السريرية لمؤشر رصد عمق التخدير Bispectral Index (BIS) للتقليل من حالة الوعي أثناء خضوع المرضى لمختلف العمليات الجراحية الاختيارية تحت تأثير المخدر العام – دراسة محتملة عشوائية – مزدوجة التعمية – ومراقبة

إعداد

تسنيم طرايرة

إشراف

د.عائدة القيسي

الملخص

مقدمة: التخدير هو حالة من فقدان الوعي الناجم عن إعطاء الأدوية المخدرة للمريض، حيث يفقد المريض ادراكه ولا يستجيب للتحفيز، وأحيانا تحدث حالة الوعي اثناء العملية الجراحية، حيث يتذكر المريض الأحداث التي حصلت خلال العملية الجراحية. إن وعي المريض تحت تأثير التخدير العام وتذكره لما حدث خلال العملية الجراحية يكون كتجربة المريض لأحداث مروعة قد تترك صدمة نفسية دائمة، وقد يكون هناك إدراك سمعي ولمسي لدى المرضى يرافقه الشعور بالعجز، وعدم القدرة على التحرك، وألم، وذعر قد يتحول إلى الخوف والفزع من الموت. يستخدم BIS كشاشة لقياس عمق التخدير للمساعدة في توجيه معايرة الأدوية، وقد أظهرت مراقبة BIS حدوث تقليل للوعي وتحسين أوقات الصحوة من التخدير العام.

الأهداف: تهدف الدراسة إلى تقييم الفعالية السريرية المراقبة باستخدام BIS للتقليل من نسبة حالات الوعي وصلته بمقاييس الدورة الدموية، استهلاك أدوية التخدير، وقت الافاقة، ونهاية وجود المخدر في الدم لدى المرضى البالغين الذين يخضعون لأنواع مختلفة من العمليات الجراحية تحت التخدير العام.

منهج البحث: تم استخدام تصميم محتمل عشوائي، مزدوج التعمية، ومراقب لهذه الدراسة، حيث شملت مجموعة الدراسة تسعة وخمسون مريضا من البالغين مع الحالة الفيزيائية للمريض درجة 1–3، تتراوح أعمارهم بين 18–72 عاما، توزيع الذكور (عدد = 41)

والإنـاث (عـدد = 18)، والمقـرر لهـم إجـراء عمليـات جراحيـة مختلفـة تحـت تـأثير التخـدير العام، وقد تم اختيار عينات الدراسة عشوائيا لاستخدام BIS لإرشاد عملية التخدير (عدد = 30) بقيم60 – 40 BIS، والتـي تعتبـر مناسـبة للتخـدير الجراحـي، أو الرعايـة الروتينيـة(RC)، التـي لا تسـتخدم) BIS عـدد = 29)، وقد تـم وضـع مجسـات الاستشـعار لجهاز BIS علـى جبين المرضـى، وتـم قيـاس معـايير الـدورة الدمويـة قبـل التخـدير و كـل 5 دقـائق خـلال هـذه العمليـة حتـى اخـراج أنبـوب التـنفس، ثـم قـيم مراقـب خـارجي (لـيس لـه علـم بهويـة العينـة) المرضـى خـلال 24–36 سـاعة بعـد الجراحـة، كمـا قامـت لجنـة مسـتقلة لـيس لها علم بهوية العينة بتقييم كل تقرير له علاقة بحالة الوعي للمرضى.

النتـــائج: كـان هنـاك فـروق ذات دلالـة إحصـائية فـي مسـتوى الـوعي بـين مجموعـة الرعايـة الروتينيـة (8/29 RC) بنسـبة 27.6%، والمجموعـة المسـتخدمة لمؤشـر قيـاس عمـق التخـدير (2/30 BIS) بنسبة 6.7(P=0.032) % ، أمـا مجموعـة خفض التخـدير الموجهـة بمؤشـر قيـاس عمـق التخـدير كانـت بنسـبة 20.9٪ (95(40%-1.4%)CI%، وكـان هنـاك فـروق ذات دلالـة إحصـائية فـي متوسـط جرعـة دواء التخـدير المستنشـق بـين مجموعـة الرعايـة الروتينـي)(RC) المتوسـط والانحـراف المعيـاري 0.029±0.008) و مجموعـة مؤشـر قيـاس عمـق التخـدير)(BIS)المتوسـط والانحـراف المعيـاري 0.025±0.009(.P=–0.023 وهنـاك فـروق ذات دلالـة إحصـائية فـي اسـتخدام الفنتانيـل بـين المجمـوعتين: مجموعـة مؤشـر قيـاس عمـق التخـدير (المتوسـط والانحـراف المعيـاري 115.56ملغـم ± 94.18) و تـم تخفيضـها إلـى (77.76 المتوسـط والانحـراف المعيـاري 77.76 ملغـم ± 40.523) لمجموعـة الرعايـة الروتينيـة، P=–0.035، وتـم خفـض نسـبة تحـرك المـريض خـلال العمليـة الجراحيـة مـن 27.6 % فـي مجموعـة الرعايـة الروتينيـة الـى 6.9% فـي مجموعـة مؤشـر قيـاس عمـق التخـدير، P=–0.037، أمـا وقـت النطـق (الكـلام) لمجموعـة العنايـة الروتينيـة كانـت (المتوسـط والانحـراف المعيـاري 12.82± 6.11) دقيقـة، وانخفضـت الـى (المتوسـط والانحـراف المعيـاري 10.21± 5.127) دقيقـة لمجموعـة مؤشـر قيـاس عمـق التخـدير، P=–0.026، وقـد سـجل المسـتوى المتوسـط للألـم

لـدى 25% لمجموعـة العنايـة الروتينيـة و صـفر لمجموعـة مؤشـر قيـاس عمـق التخـدير، P=−0.011، كمـا أن هنـاك فـروق ذات دلالـة إحصـائية بـين المجمـوعتين فـي وقـت الخـروج مـن وحـدة العنايـة مـا بعـد التخـدير وهـي (المتوسـط والانحـراف المعيـاري 12.28 ± 4.989) دقيقـة لمجموعـة العنايـة الروتينيـة و (المتوسـط والانحـراف المعيـاري 9.23 ± 3.819) دقيقة لمجموعة مؤشر قياس عمق التخدير، 0.007. − = Pوهناك فروق ذات دلالـة إحصـائية بـين المجمـوعتين خـلال العمليـة فـي قـيم ضـغط الـدم الانقباضـي والانبساطي ومتوسط ضغط الدم خلال اوقات مختلفة من العملية.

الاسـتنتاجات: إن اسـتخدامBISيمكـن أن يقلـل مـن حـدوث حالـة الـوعي أثنـاء التخـدير العـام للمرضـى الـذين يخضـعون لأنـواع مختلفـة مـن العمليـات الجراحيـة. إن الإدارة الموجهـة لـ BIS يمكـن أن تكـون أفضـل مـن الرعايـة الروتينيـة للتقليـل مـن اسـتهلاك المخـدر العـام، وأوقـات الانعـاش مـن التخـدير، وتغيـرات الـدورة الدمويـة، لـذا ينبغـي أن تكـون الوقايـة مـن حالـة الـوعي للمـريض أثنـاء الجراحـة قـرارا مهمـا يتخـذه أطبـاء التخـدير مـن خـلال ممارساتهم.

آثـار التخـدير: لا تُسـتخدم (تقنيـة الـ BIS لرصـد عمـق التخـدير) بانتظـام فـي أقسـام التخـدير فـي فلسـطين علـى الـرغم مـن أن أغلبيـة ممرضـي التخـدير علـى وعـي تـام بهـذه التقنيـة والغـرض منهـا، ومـن المهـم أن يكـون أخصـائي التخـدير علـى علـم بهـذه التقنيـة وكيفيـة البـدء باسـتخدامها مـن أجـل توحيـد إجـراءات التخـدير السـريرية فـي غرفـة العمليـات لتحسـين الرعايـة المقدمـة للمرضـى، ومـن المهـم أيضـا تقـديم هـذه التقنيـة لطـاقم أقسـام التخـدير فـي فلسطين.

كلمات مفتاحية: الوعي، التخدير العام، مؤشر رصد عمق التخدير(BIS)