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The Effect of Dexmedetomidine versus Midazolam on Awareness in Cesarean Section under General Anesthesia

Thesis

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List of Abbreviations

Abbr.	Full Term
ASA	American Society of Anaesthesiologists
AV	Atrioventricular
BIS	Bispectral index
BKCa	Potassium channels calcium-activated
BP	Blood pressure.
BSR	Burst Suppression Ratio.
BZDs	Benzodiazepines.
CNS	Central nervous system.
CS	Cesarean section.
ECG	Electrocardiogram.
EEG	electroencephalogram
ETAC	End-tidal anaesthetic concentration.
GABA	Gama aminoputeric acid
HR	Heart rate.
Hz	Hertz
IDT	Induction to delivery time
IV	intravenous

KATP .....Potassium channels adenosine triphosphate-sensitive.

KV .....Potassium channels voltage-dependent () channels

MAC .....minimum alveolar concentration.

NAP-5 .....The fifth National Audit Project.

NICE .....The National Institute for Health and Clinical Excellence.

NMBA .....Neuromuscular blocking agent.

PTSDs .....Post-traumatic stress disorders.

RE.....Response entropy.

SD .....Standard Deviation.

SE .....State entropy.

TIVA .....Total intravenous anesthesia.

UDT .....Uterine incision to delivery time

α2-AR .....alpha2 adrenoceptor

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INTRODUCTION

Anesthesia awareness is defined as the unintended experience and explicit recall of intraoperative events. The incidence of intraoperative awareness was reported to be 1.2% in 1960. Recent studies showed the incidence to be 0.1-0.2% in low-risk surgical procedures (***Sebel et al., 2004)***; however, it can reach 1% for patients at increased risk e.g cesarean section delivery, multiple traumas, cardiac surgery, difficult intubation and patients with a previous history of awareness ***(Lopez et al., 2007)***. Intraoperative awareness is a potentially psychologically devastating complication of anesthesia associated with a high incidence of psychological sequelae, with post-traumatic stress disorders (PTSDs) being the most severe and causing high public concern, increases patients' apprehension of surgery and leads to medical-legal issues regarding anesthesia (***Leslie et al., 2010).***

Cesarean section (CS) under general anesthesia renders parturient patients at increased risk of inadequate anesthesia resulting in intraoperative awareness and subsequent recall higher than that reported in a general surgical population (***Sandin et al., 2000)***. This is because of rapid sequence induction, avoidance of opioids and benzodiazepine until the delivery of the newborn and limited

volatile concentration by 30 – 40% due to increased respiratory minute volume, decreased functional residual volume and secretion of endorphins and progesterone. Due to the effect of inhalational anesthetics in decreasing uterine contractility and tone in a dose-dependent manner, their MAC are continued to be limited even after fetal expulsion (***M-S CHANG1., 2009).***

Preventing intraoperative awareness in patients undergoing general anesthesia can be challenging for an anesthesiologist. Although monitoring methods are available, recognition of intraoperative awareness is difficult because the awareness recall can be identified only postoperatively by obtaining information directly from the patient. Conventional indicators of physiological and motor responses, such as high blood pressure, rapid heart rate, movement, sweating, or lacrimation are not adequately sensitive and specific and often masked by the neuromuscular blocking agents as well as the concurrent administration of other drugs such as beta-blockers or calcium-channel blockers. To overcome the limitations of existing methods, new techniques of detecting intraoperative awareness that are less affected by the drugs are being developed. These devices focus on measuring brain activity rather than physiological responses; these EEG devices include the Bispectral Index (***Myles et al., 2004)***

The Bispectral Index (BIS) is an empirically derived electroencephalographic parameter measuring the hypnotic component of anesthesia that guides the administration of volatile anesthetics. It calculates an index using a proprietary algorithm based on a single channel of frontal EEG activity. The algorithm calculates an index using EEG time domain (burst-suppression analysis) and frequency domain (power spectrum). This index is scaled between 0 (isoelectrical activity) and 100 (awakened state), indicating the hypnotic level. Specific ranges (40-60) were recommended to reflect a low probability of awareness with recall during general anesthesia (***Hyun Sik, 2014).***

Dexmedetomidine is a highly selective alpha2 adrenoceptor (α2-AR) agonist recently introduced to anesthesia practice. It produces dose-dependent sedation, anxiolysis and analgesia (involving spinal and supraspinal sites) without respiratory depression. Dexmedetomidine has been widely used in anesthesia as a premedicant analgesic to attenuate a sympathetic response to surgery in the perioperative period by stimulating central α2 and imidazoline receptors, and to potentiate the anesthetic effects of all intraoperative anesthetics. In pregnant women it doesn't cross uteroplacental barrier due to its high placental extraction. Dexmedetomidine has been used as a sole

sedative for noninvasive procedures and as an adjunct for invasive procedures ***(Abhijit et al, 2013)***. There was also an acceptable recovery time with it. Therefore, dexmedetomidine may provide an effective alternative to currently used anesthetic regimens for patients in various surgical settings. It is the dextrorotatory S-enatiomer of medetomidine. Dexmedetomidine is a very useful addition to the family of drugs used in anesthesia (***A. Palanisamy et al, 2009).***

Midazolam is a water-soluble benzodiazepine. It binds receptors at several sites within the CNS, including the limbic system and reticular formation. Its effects may be mediated through GABA receptor system; increase in neuronal membrane permeability to chloride ions enhances the inhibitory effects of GABA. It has anxiolytic, amnestic, and hypnotic properties and boasts a short elimination half-life of roughly 1 to 4 hours, has clinically inactive metabolites. It is painless upon injection. Further, it decreases analgesic requirements and diminishes agitation without cardiovascular depression. However, significant respiratory depression, particularly when used in combination with opioids, and postoperative psychomotor and cognitive impairment warrant caution during its administration. With regard to the obstetric population, midazolam crosses the

placenta, enters fetal circulation, and may contribute to neonatal depression (***M-S CHANG1, 2009).***

Midazolam produces a maximal effect 3 – 5 min after administration and a long amnesiac period of 20 – 30 min. It may, therefore, be a candidate drug for decreasing the need for inhaled anesthetics while still maintaining low BIS (***Maze et al, 2001).***

AIM OF THE WORK

The aim of this study is to investigate the effect of dexmedetomidine versus midazolam in reducing the risk of awareness guided by the bispectral Index when they are used as an adjuvant with general anesthesia after fetal expulsion in cesarean section.

Chapter (1)

AWARERNESS IN ANESTHESIA

The phrase awareness with recall refers to both intraoperative consciousness and explicit recall of intraoperative events. The most important contributing factor for awareness is under dosing of anaesthetic agents relative to the patient's specific requirements. Although the incidence of awareness may be reduced with preventive measures, it may not be eradicated completely. Thus, all patients undergoing general anesthesia should be informed that awareness is rare, but can occur ***(Mashour GA, et al, 2009).***

Incidence:

Awareness experiences range from isolated auditory perceptions to reports of a patient being fully awake, immobilized, and in pain. Incidence of awareness varies widely due to methodological differences in postoperative assessment of awareness and differences in anaesthetic practice ***(Mashour GA, et al, 2009).*** Although the most common outcome measured is postoperative recall for the awareness event, intraoperative consciousness and explicit recall of intraoperative events may be dissociated from each