A PROSPECTIVE DOUBLE-BLIND RANDOMIZED CONTROLLED TRIAL ON THE EFFECT OF DEXMEDETOMIDINE TOWARDS PREVENTING EMERGENCE AGITATION IN PATIENTS UNDERGOING GENERAL ANAESTHESIA FOR LIMB SURGERIES

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INTRODUCTION

CHAPTER 1 : INTRODUCTION

1.1 Research Background

Sikich and Lerman (2004) defined emergence delirium as “a disturbance in a patient’s awareness of and attention to his or her environment with disorientation and perceptual alterations, including hypersensitivity to stimuli and hyperactive motor behaviour in the immediate postanaesthesia period.” In most literature, emergence agitation and emergence delirium have been used conversely. Emergence agitation is not a new clinical phenomenon, with various predisposing factors and effects; however, it is of more importance recently because its increasing incidence seem to coincide with more widespread use of sevoflurane in recent years.

Other possible known causes of emergence agitation are pain, preoperative anxiety, type of surgical procedures, personal characteristics of the patient and type of anaesthetics. However, the exact cause and mechanism is still unknown.

Emergence agitation at the end of anaesthesia may make the anaesthetist look bad and seemingly lacking of experience or skill, just like a pilot who had just made a rough landing of a plane. It can cause distress for the anaesthetist and nursing team, resulted in more manpower required in the recovery unit and can hamper proper postoperative monitoring and management. More seriously, it can result in dangerous consequences too such as suture dehiscence, bleeding, increased pain, hypertension and increased intracranial pressure, self extubation, accidental removal of catheters and drains, and also injury to the patient’s self and to staff.

Drugs such as analgesics, opioids, benzodiazepines, clonidines and dexmedetomidine have been used either prophylactically or as a treatment for emergence agitation with variable success (Isik et al., 2006).

1.2 Rationale of Study

Due to the problems and complications from emergence agitation as mentioned, it is a concern that methods to reduce the incidence of emergence agitation be researched and applied.

This study is to evaluate the benefits, if any, of dexmedetomidine to reduce or prevent emergence agitation and to determine the possibility and the severity of its side effects when used as an infusion intraoperatively. Drugs such as analgesics, opioids, benzodiazepines, clonidines also had been studied before but these drugs are less practical to be used in this setting as they have respiratory depressant effects and may cause delayed awakening from general anaesthesia.

Usage of a specific drug as prevention for emergence agitation is still not a common practice in our routine of anaesthesia. If it is proven to be beneficial and safe, this practice should be encouraged and implemented in our general anaesthesia regime, particularly for those with high risk of serious sequelae from emergence agitation such as tonsillectomy, corneal implants and neurosurgery patients, and also patients with cardiac diseases and hyper reactive airways. Studying the risk factors for emergence agitation may enlighten us of the high risk group for us to anticipate and

treat pre-emptively. We suggest that emergence agitation be addressed and treated equally the way we usually anticipate and pre-emptively treat other common anaesthetic problems such as postoperative pain or postoperative nausea and vomiting.

LITERATURE

REVIEW

CHAPTER 2 : LITERATURE REVIEW

2.1 Emergence from Anaesthesia

Darren et al. (2014) defined emergence as the wake-up period following withdrawal of general anaesthetic, the period from the cessation of general anaesthetic agents until the patient is able to make a non-reflex response to verbal command.

There has been an increasing interest in anaesthetic emergence and the neurobiological processes leading to the return of consciousness over the last decade. Patients characteristics and changes that take place during emergence has captivated the attention of researches who tried to unravel the mystery of emergence from the neural correlates of consciousness to clinical oriented studies such as patient's quality of recovery and factors that can affect them. Apart from scientific interest, studies regarding emergence from anaesthesia has been gaining popularity with the aim to improve the clinical course during anaesthesia, particularly during emergence as it is a fact that emergence is an important phase, whereby major life-threatening complications can occur such as bronchospasm and bronchial asthma, severe hypertension, intracranial bleed and myocardial infarction if it is not handled well. A smooth and an uneventful emergence should be one of the main aims of anaesthetists conducting general anaesthesia in the operating theatre.

When a patient is induced to loss of consciousness through anaesthesia, he or she goes through several stages. At a small dose, anaesthetics first suppress thinking,

focused attention, and working memory. As the dose is increased, consciousness and voluntary responsiveness begin to fade. When subjects no longer respond to verbal stimulation, it is presumed that their consciousness is gone. This is a conjecture supported by the loss of episodic memory of the stimuli, but does not define the residual mental contents of the subject at the time of stimulation. As the anaesthetic dose is increased, nociceptive and autonomic reflexes are suppressed. The latter are mediated at the brainstem and spinal level and are thought to occur after the loss of consciousness. At even higher dose, brain electrical activity is turned into intermittent, and ultimately, complete suppression. For the time being, loss of consciousness will be operationally defined as a loss of voluntary responsiveness, excluding limiting factors such as the use of muscle relaxants, the presence of motor impairment, or akinetism. At an anesthetic depth characterized by the subjects' unresponsiveness, a partial, but not complete, reduction in connectivity is generally observed. Functional connectivity of the frontoparietal association cortex is often reduced, but a causal role of this change for the loss of consciousness remains uncertain. Functional connectivity of the nonspecific (intralaminar) thalamic nuclei is preferentially reduced by propofol. Higher-order thalamocortical connectivity is also reduced with certain anesthetics. Anaesthetic loss of consciousness is not a block of corticofugal information transfer, but a disruption of higher-order cortical information integration. (Hudetz, 2012).

Multiple neurotransmitter system contribute to wakefulness, however none functions as a sole player. They are interconnected to each other to form an excitatory network and act with interactions before projecting to the cortex. Among the neurotransmitter system that are involved are the cholinergic (acetylcholine) basal

forebrain, orexinergic lateral hypothalamic, serotonergic raphe, noradrenergic locus coeruleus, and histaminergic tuberomammillary neurons. These neurotransmitters are involved in the mechanism of anaesthesia, during induction, maintenance and emergence (Muller et al., 2011).

Previously, there was a common belief that emergence from anaesthesia is the inverse or mirror process of induction, brought about simply by elimination of anaesthetic drugs from their sites of action in the central nervous system. However, recent studies had proven that emergence from anaesthesia is a unique process by itself, a process with a distinct neurobiology characteristics from anaesthesia or loss of consciousness.

Firstly, from neuroimaging, it can be seen that different areas in the brain is activated during induction of anaesthesia (loss of consciousness) and emergence. A human study with positron emission tomography indicated several brain regions are activated in the consciousness state. The regions are the anterior cingulate cortex in the medial frontal lobe, the midline thalamus, hypothalamus, the locus coeruleus or parabrachial area in the brainstem, the cerebellum, and portions of the lateral orbital frontal and parietal lobes. When the subjects are conscious, functional connectivity exists between the frontal and parietal brain areas, but that connectivity fades in conjunction with loss of consciousness from anaesthetics. The return to consciousness was not associated with a significant restoration of cortical activation. In fact, arousal induced activations were mostly localized in deep, phylogenetically old brain structures rather than in the neocortex (Langsjo et al., 2012).

Kelz and colleagues in a study published in 2008 mentioned that there are important differences in the neural substrates mediating induction and emergence. They studied the role of the endogenous orexinergic system in impacting from, but not entry into the anaesthetized state. From their study, they demonstrated that isoflurane and sevoflurane, two commonly used general anesthetics, inhibit c-Fos expression in orexinergic but not adjacent melanin-concentrating hormone neurons; suggesting that wake-active orexinergic neurons are inhibited by these anesthetics. Genetic ablation of orexinergic neurons, which causes acquired murine narcolepsy, delays emergence from anesthesia, without changing anesthetic induction. By this they were able to distinguish the mechanisms of induction from those of emergence. Thus the newer concept that emergence also depends on recruitment and stabilization of wake-active region in the brain.

A study done by Hudetz et al. in 2012 also supports the theory that emergence is an active process altogether, not merely a reverse process from anaesthesia or losing of consciousness. In this study, a substantial asymmetry in regional thalamocortical functional connectivity was observed during wakefulness before and after propofol sedation was given. After the participants had regained consciousness, they demonstrated that the functional connectivity of several thalamocortical networks was increased well above the preanesthetic baseline. Thus, this was interpreted as a probable recruitment of additional neural resources as required for the restoration of conscious functionalities of the brain.

2.2 Emergence Agitation. Definition. Background. Significance

Emergence means liberation from or when a patient is awakening from the state of anaesthesia when at the end of surgery anaesthesia is no longer needed and terminated. Agitation is a condition where there is some form of restlessness and mental distress. Emergence agitation is first described in the 1960s, whereby children encounter a wide range of behavioural disturbances, including sobbing, crying, thrashing and disorientation when they had just emerged from anaesthesia. Emergence delirium can be defined as a state of mental confusion, agitation and disinhibition marked by hyperexcitability, crying, restlessness and hallucinations during emergence from general anaesthesia (Stamper et al., 2014).

In the literatures, the terms emergence agitation and emergence delirium were used interchangeably. The reported prevalence of emergence agitation or delirium varies widely among the literature, ranging from 10% to 80% (Kwak, 2010). Numerous literatures mentioned that the problem with emergence agitation is the inadequate exact tool or objective method for assessing it. There are different scales available to measure agitation such as the Riker agitation-sedation scale, the Richmond sedation-agitation scale and the New Sheffield sedation scale with the first two having excellent inter-rater reliability. However these scales are validated for use in the ICU and not validated in the recovery room or PACU (Yu et al., 2010).

Ideally emergence should occur in a short time frame and in a smooth fashion, without the undesirable reaction from the patient and without unwanted side-effects from the residuals of the anaesthetics and their resultants in the physiology pertinent

to the anaesthetists which involve the airway, respiration, hemodynamics, autonomic, metabolic and endocrine functions. Though there has been better comprehension of arousal pathway in the nervous system along with the introduction of newer agents of anaesthetics and reversal plus modern monitoring systems resulting in faster and smoother emergence, anaesthetists still have challenges as patients' responses to emergence are still widely variable with a number of predisposing factors (Bhaskar, 2013). Furthermore, the underlying causes and the exact mechanisms of emergence agitation are still not clearly understood (Kwak, 2010).

Emergence agitation can cause a huge stress for the anaesthetist and team, also for the patient and family. The failure to restrain and manage the patient in the agitated and sometimes uncontrolled situation added by the inability to comprehend it not only cause physiological distress to the anaesthetist but also poses risk of injury to the patient and also to the anaesthesia personnel (Lepouse et al., 2006; Sikich and Lerman, 2004). What could happen during this time is the patient may be pulling IV lines and drains, self extubate and causing self harm and other bodily injuries (Wofford & Vacchiano, 2011). It can also hamper proper monitoring and complicate management of the patients in the post anaesthesia care unit or recovery unit, requiring more staff for support (Voepel-Lweis et al., 2003). Seeing their loved ones in a very agitated state in the post-operative period may be terrifying for the family members as they may think that the patient had been through a difficult and problematic operation and anaesthesia. It is not easy on the family members too if they had to see the patient being put on physical restraint.

2.3 Causes and Risk Factors for Emergence Agitation

There is no known definitive cause for emergence agitation. But there are possibilities that pain, preoperative anxiety, types of procedure, patient's personality and characteristics, and anaesthetic types can explain emergence agitation, although there is no known sole determining factor (Vlajkovic & Sindjelic, 2007).

Isoflurane, sevoflurane and desflurane are the newer gaseous anaesthetic agents that has been created to allow smoother and more predictable emergence due as they allow rapid titration of depth of anaesthesia compared to the older generation agents such as ether and halothane. However, with widespread usage of sevoflurane, there is reported increase in incidence of emergence agitation (Beskow & Westrin, 1999). Also when compared to propofol, patient who had gets sevoflurane as anaesthetic had more incidence of emergence agitation (Kanaya et al., 2013). The characteristic of sevoflurane which has low blood solubility thus resulting in rapid removal is identified to be one of the mechanisms of emergence agitation caused by sevoflurane (Cravero et al., 2000). However, due to a superior elimination of propofol and remifentanil in terms of rapidity and completeness, patients received total intravenous anaesthesia have less emergent agitation compared to patients received general anaesthesia by inhalational agents

Smessaert and colleagues construed two main causes for emergence agitation. The first one being anaesthetic cause (higher incidence in cyclopropane compared to ether or barbiturates) and the second one being surgical factor (higher incidence in peripheral surgery compared to intra-thoracic and intra-abdominal surgery). The

emergence agitation is more related to the patient's characteristics (gender, age, mental attitude). A final hypothesis was made that rather than pain, the patient's personality is the more important element that determines whether the patient will experience emergence agitation.

There are a lot of studies about emergence from anaesthesia conducted and mostly showed that women recover faster than men and that there are differences in the post-operative recovery profile between the two sexes. Women have lighter anaesthetic states and faster recovery when compared to men, given the same amount of anaesthetic agents and opioid analgesic intra-operatively (Buchanan et al., 2011). Sex hormones seem to have a role in modulating these differences. Estrogen, progesterone and androgen receptors have been recognised in brain which has roles different from reproductive functions. While progesterone has hypnotic effects via direct action on the GABA receptor, estrogen on the other hand suppresses this receptor resulting in opposite effect (Manber and Armitage, 1996). Furthermore, estrogen acts at NMDA-type glutamate receptors by increasing the excitatory transmission and increasing the affinity of glutamate to NMDA receptors (McEwen and Alves, 1999). These explain why women have more rapid emergent compared to men. However, more pertaining to emergence agitation (as it is often related to pain), there are difference in nociception in between male and females. Estrogen and progesterone had been observed to mediate and play a role in effecting excitability in brain and spinal cord (Woolley and Schwartzkroin, 1998). Though women have faster emergent, the quality is poorer due to higher pain scores (Buchanan et al., 2011). However there are different studies that showed the exact opposite. Men have lower

pain threshold compared to women (Tsui et al., 1996). And there is a higher incidence of emergence agitation in males, probability due to lower pain threshold. Pain is evidently one of the main cause of emergence agitation, as it showed that patients who were given adequate post-operative analgesia has lower incidence of emergent agitation compared to patients without post-operative analgesia (Yu et al., 2010).

Type of surgical procedures also has an influence to the quality of emergent. Operations on the oral cavity and ENT are a risk factor for emergence agitation in children (Voepel-Lewis et al., 2003). It is speculated that head ENT surgery is related to emergence agitation as these patients feels suffocated during the emergent period (Eckenhoff, 1961). In a study by Lepouse et al. in 2006, it is found that emergence agitation is more common in abdominal and breast surgery.

Inadequate reversal of muscle relaxant is also one of a known cause of emergence agitation in which patient wakes up with a feeling of suffocation and helplessness causing apprehensive behaviours. Others mentioned the presence of endotracheal tube and distended bladder when the patient wakes up as identified causes.

Contradictory results had been yielded from previous studies regarding whether duration of anaesthesia influences emergent behaviour (Wells and Rasch, 1999). Some studies observed that shorter duration of anaesthesia has higher incidence of emergence agitation, some studies found the opposite is true and some studies dictated that anaesthetic duration has no impact. It is postulated that shorter surgery allows rapid washout of anaesthetics from the body causing rapid emergence,

and emergence agitation resulted because effects of the analgesics given intraoperatively have yet to take peak effect (Rahil et al., 2012).

Patients given midazolam preoperatively to alleviate anxiety had shown to have higher incidence of emergence agitation due to the paradoxical effect (Kudoh A et al., 2004) while patients on antidepressants has a protection from delirium as these anxiolytics have a long half life. Patients who have history of medical illness and are accustomed to hospital environment found to have protective point against emergence agitation (Lepouse et al., 2006).

Preoperative anxiety is an inconsistent risk factor for emergence delirium. A study done by Lepouse and colleagues in 2006 had found no correlation between preoperative anxiety and emergence agitation while Kain ZN and colleagues in their study conducted in 2004 among children undergoing surgery found that there is a relationship between anxiousness and emergence delirium.

2.4 Prevention and Treatment for Emergence Agitation

Simple actions such as removing endotracheal tube as early as possible and bladder drainage before patient wakes up, also explaining regarding various tubes and drainage that the patient may find him or herself connected to on waking up to reduce surprise and anxiety may reduce emergence agitation. Pain must be addressed, treated pre-emptively and aggressively (Lepouse et al. 2006).

There are many studies conducted regarding drug choices to tackle emergence agitation. Drugs that have been studied include fentanyl, propofol, clonidine and dexmedetomidine. Lee and colleagues in 2010 studied whether there is clinical benefit of propofol 1mg/kg given at the end of surgery in reducing the incidence and severity of emergence agitation in patients undergoing adenotonsillectomy, but they had found that it has no effect. Though as mentioned earlier that patients given TIVA propofol have better recovery profile and less occurrence of emergence agitation compared to patients who receive gaseous agents, the failure of propofol bolus given in this study to attenuate emergence agitation maybe attributed to the low dose (1mg/kg) and rapidly metabolised (Dahmani et al., 2010).

Opioids have been investigated for their useful actions in smoothening emergence, but it mainly by suppressing cough that are seen during emergence when desflurane is used. For this, short acting opioids such as alfentanil and sulfentanil are used and they are given as a bolus dose at the end of surgery (Lee MG et al., 2011 and Lee JY et al., 2012).

Benzodiazepines such as midazolam though given to patients to alleviate anxiety and expected to protect from delirium surprisingly increased the odds of emergence agitation. This is because they are known to have paradoxical effects and can cause irritability, aggressiveness and confusion (Kudoh et al., 2004). However there are studies that showed midazolam has benefit in reducing the incidence of emergence such as the one by Schor and colleagues in 1994. Thus, the effects of midazolam in curbing emergence agitation are not consistent.

Dexmedetomidine had been shown to have positive effects in reducing or prevent emergence agitation in various studies.

2.5 Dexmedetomidine – A Review

Dexmedetomidine is an imidazole compound which is a pharmacologically active dextroisomer of medetomidine (Savola and Virtanen, 1991). Dexmedetomidine is a potent α2-adrenoceptor agonist, the same with clonidine but with 8 times higher affinity. Its action is mediated through postsynaptic α2-adrenoreceptor that activate pertussis toxin sensititve G-proteins, resulting in increased conductance through potassium ion channel (Salonen et al., 1997). It is the α2-adrenoceptor that is responsible in relaying the properties of sedation and analgesia in dexmedetomidine.

With a target plasma concentration of 0.6g/L, dexmedetomidine has a volume of distribution at steady state of 1.33L/kg and clearance of 0.495L/h/kg. Its distribution half-life is 6 minutes and elimination half-life is 2 hour. It is excreted mainly in the kidney (95%) as methyl and glucuronide conjugate (Nilla et al., 2000).

Since its release in 1999, it had gained popularity in all age groups of patients that needs sedation, mostly because of its special feature of not causing respiratory depression, also due to its good profile in neuroprotection, cardioprotection and nephroprotection that had been proven in many studies (Chrysostomou and Schmitt, 2008). Its main indication is for sedation of patients in ICU and shown to reduce the requirement of analgesics for post-operative patients. It has sedative, analgesia and

anxiolytic effects while maintaining arousability and cooperation, thus it is more known for its ability to produce 'conscious sedation' – a unique feature compared to other sedation such as propofol, benzodiazepines and opioids. In a phase I study, a dose dependent increase in sedation was seen with infusing dexmedetomidine for 24 hours with target plasma concentrations of 0.3, 0.6 and 1.25mcg/L. Though there is differences of depth and duration of sedation between the groups, all healthy volunteers showed the same level of arousability and cooperation despite achieving clinically effective sedation (Morrison et al., 1991). In clinical trials too dexmedetomidine showed efficacy in providing sedation to patients. In two phase II studies, dexmedetomidine showed significant reduction of the need to give rescue sedation (midazolam and propofol) in postsurgical patients requiring ventilation and sedation (Bachand et al., 1999 and Martin et al., 1999). As for analgesic property, dexmedetomidine in the same studies done by Bachand and Martin in 1999 is found to reduce the need for rescue analgesic in postsurgical ICU patients requiring mechanical ventilation and sedation. In the study done also showed patients on dexmedetomidine are calmer and less anxious than their placebo counterparts. This anxiolysis effect of dexmedetomidine resulted in patients who are easier to manage.

Among the pharmacodynamic effects of dexmedetomidine, 1mcg/kg infused over 2 minutes caused significant maximum reduction in heart rate and blood pressure, coinciding with reductions in plasma level of noradrenaline and adrenaline (Bloor et al., 1992). In 2 phase III trials with patients receiving dexmedetomidine infusion of 0.2-0.7mcg/kg/h, consistent reduction in mean blood pressure and heart rate seen, with return to baseline seen after 6 hours stopping infusion (Grounds 1999).

Dexmedetomidine 2mcg/kg infused over 2 minutes in healthy males resulted in slight increase in carbon dioxide partial pressure (reduction in about 5mmHg over 10 minutes and gradually returned to normal after that) and decrease in minute ventilation (about 6-8L/min which occurred after 60 minutes). There was minimal change in respiratory rate. Respiratory depression is not an issue with dexmedetomidine. In phase 1 study, 24 hour infusion of dexmedetomidine with target plasma concentration of 0.3-1.25mcg/L did not result in respiratory depression in volunteers; with good oxygen saturation maintained seen. There is also no difference seen in the respiratory rate post extubation between dexmedetomidine and placebo group (Belleville et al., 1992).

As of its side effects and tolerability, dexmedetomidine has a fairly good profile. In a phase III study done before, the most common side effects related to dexmedetomidine were hypotension, hypertension, nausea, bradycardia and dry mouth compared to placebo patients, who had reduced incidence of the mentioned side effects except for hypertension (Nilla et al., 2000). However, in most studies done previously, they are minimal, only occur in high infusion rates and usually counteracted successfully with resuscitating drugs. Such hemodynamic effects may be expected to be more pronounced and severe in hypovolaemic patients, in those with diabetes mellitus or chronic hypertension and in the elderly (Lee 2012). Dexmedetomidine also does not result in delayed recovery or prolonged extubation time (Kang et al., 2012).

2.6 Dexmedetomidine in Preventing Emergence Agitation

Dexmedetomidine is widely used in the ICU setting. The use of it in the operating theatre setting and in patients undergoing surgery is not a current trend due to the concerns of intraoperative hemodynamic instability (bradycardia and hypotension) and postoperative delay in recovery (Lee, 2012). However, numerous studies had proven successful use of dexmedetomidine perioperatively for multiple objectives (e.g. attenuation of stress response of intubation, etc) without significant side effects, and this includes its use to prevent or attenuate emergence agitation. The stable intraoperative hemodynamics and postanaesthetic recovery speed that is acceptable are thought to be resulted not by the pharmacologic effect of dexmedetomidine but by its anaesthetics-sparing effect (Kang et al., 2012).

In a study done by Kim and colleagues in 2013, intraoperative continuous dexmedetomidine infusion until extubation was effective in reducing the incidence of emergence agitation after nasal surgery without delay of extubation or increasing incidence of other complications.

In children undergoing tonsillectomy and adenoidectomy, an intraoperative initial loading dose of 2mcg/kg dexmedetomidine followed by an infusion at 0.7mcg/kg/h decreased intraoperative opiate and anaesthetic requirements and decreased opiate requirements in the PACU, compared to the control group receiving intraoperative IV fentanyl. Additionally, there was a significantly lower incidence and duration of severe emergence agitation in children who received dexmedetomidine (Patel et al., 2010).

A study was done by Kavalchi and colleagues and published recently in 2013 comparing the effects of dexmedetomidine and remifentanil on emergence agitation after sevoflurane anaesthesia in adults undergoing septoplasty. In this study, both dexmedetomidine and remifentanil was given as infusion intraoperatively. Dexmedetomidine infusion dose was 0.4mcg/kg/hour after a loading dose of 1mcg/kg for 10 minutes given. The incidence of emergence agitation and postoperative pain score was similar between the 2 groups with stable hemodynamics intraoperatively.

Children undergoing tonsillectomy experienced smoother emergence from general anaesthesia with better pain scores with infusion of 0.5mcg/kg of dexmedetomidine for 5 minutes before extubation when compared to placebo group. Lower frequency of airway difficulties was also noted in the dexmedetomidine group. This was attributed to the reduced laryngeal stimulation due to the sedative and analgesic effects of dexmedetomidine (Guler et al., 2005). In a similar study with the same paediatric population undergoing same surgery but with a lower dexmedetomidine infusion (0.3mcg/kg) also given 5 minutes prior to extubation, comparing it with propofol. It showed that dexmedetomidine was superior to propofol in reducing emergence agitation, postoperative pain score and extubation time, without affecting the length of stay in PACU (Monaz and Ashraf, 2013).

Dexmedetomidine infusion of 0.2mcg/kg/h given to children aged 1-10 years undergoing surgery under sevoflurane anaesthesia when compared to saline placebo infusion showed lower incidence and frequency of emergence agitation with comparable extubation and discharge time (Shukry et al., 2005).

There was also a study comparing different infusion rates of dexmedetomidine. In a study by Ibacache and colleagues published in 2004, where dexmedetomidine was given as a single dose for 10 minutes after intubation in children undergoing superficial lower abdomen and genital surgery, it showed that a dose of 0.3mcg/kg reduced the incidence of emergence agitation better than 0.15mcg/kg group, and in both group lower incidence of emergence agitation seen when compared to the placebo group. General and intraoperative variables were similar and no side effects to dexmedetomidine were observed.

There are many more studies done regarding the effects of dexmedetomidine in preventing or treating emergence agitation, with different modes of administration seen such as single dose after intubation, single dose just before extubation, infusion throughout operation and infusion with loading dose, also with different doses. Most of them showed success of dexmedetomidine in this term, with relatively safe profile of intraoperative hemodynamics in the lower doses range. Furthermore, dexmedetomidine showed superiority in regards to respiratory stability, extubation time and postoperative pain status compared to other agents such as opioids and propofol.

OBJECTIVES

CHAPTER 3 : OBJECTIVES

3.1 Primary Objective

General objective

- To investigate whether dexmedetomidine has positive effects in preventing emergence agitation in patients undergoing general anaesthesia

Specific objective

- To compare the incidence of emergence agitation between dexmedetomidine group and control (placebo) group

3.2 Secondary Objectives

- To evaluate whether the following are risk factors for emergence agitation
    - Patient's demographic – Age, gender, race
    - Preoperative anxiety level
    - Duration of GA
    - Type of orthopaedic procedure
        - Superficial / soft tissue / muscle
        - Involving bone structure
- To observe the presence of side effects or complications of dexmedetomidine infusion during general anaesthesia