CHILDRENS’ BEHAVIOUR AND PHYSIOLOGICAL PARAMETERS AT RECOVERY FOLLOWING DENTAL GENERAL ANAESTHESIA WITH AND WITHOUT PREMEDICATION ORAL MIDAZOLAM AT HOSPITAL UNIVERSITI SAINS MALAYSIA: A PRELIMINARY STUDY

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by

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LIST OF ABBREVIATIONS

AAPD	American Academy of Pediatric Dentistry
AAT	Animal-assisted therapy
ASA	American Society of Anesthesiologists
BSPD	The British Society of Paediatric Dentistry
DGA	Dental treatment under general anaesthesia
EAPD	The European Academy of Paediatric Dentistry
FIS	Facial image scale
GA	General anaesthesia
GABAA	Gamma-aminobutyric acid type A
Hospital USM	Hospital Universiti Sains Malaysia
HR	Heart rate
OT	Operation theatre
PACU	Post anaesthesia care unit
PECS	Picture exchange communication system
RR	Respiratory rate
SADE	Sensory-adapted dental environments
SpO2	Peripheral capillary oxygen saturation
USM	Universiti Sains Malaysia

LIST OF APPENDICES

TINGKAH LAKU DAN PARAMETER FISIOLOGI KANAK-KANAK PADA MASA PEMULIHAN SETELAH MENJALANI BIUS UMUM PERGIGIAN DENGAN MIDAZOLAM SECARA ORAL DAN TANPA PREMEDIKASI DI HOSPITAL UNIVERSITI SAINS MALAYSIA: KAJIAN AWAL

ABSTRAK

Premedikasi *midazolam* secara oral kebiasaannya diberi bagi mengawal tingkah laku dan status tingkah laku dan fisiologi pesakit kanak-kanak masih belum diterokai secara menyeluruh. Kajian ini bertujuan untuk menilai kesan premedikasi *midazolam* secara oral ke atas tingkah laku pemulihan dan kesan parameter fisiologi kanak-kanak yang menjalani DGA. Tiga puluh kanak-kanak yang tidak bekerjasama yang berumur dari 2 sehingga 11 tahun terlibat dalam kajian percubaan kawalan rawak ini. Kumpulan I menerima 0.5 mg/kg midazolam secara oral 30 minit sebelum masuk ke dalam dewan bedah, manakala Kumpulan II tidak menerima sebarang premedikasi. Parameter pisiologi diukur selepas tiba di unit penjagaan selepas bius. Tingkah laku pemulihan juga dirakamkan untuk penilaian menggunakan *Modified Houpt Rating Scale*. Tidak terdapat perbezaan yang signifikan terhadap tingkah laku dan parameter fisiologi bagi kedua-dua kumpulan ($p > 0.05$). Tiada perkaitan yang signifikan antara premedikasi *midazolam* secara oral dengan tingkah laku pemulihan yang berjaya (p=0.381). Walau bagaimanapun, aliran yang menarik bagi tingkah laku positif dan fisiologi lebih baik telah diperhatikan dalam kalangan kanak-kanak dengan premedikasi *midazolam* secara oral. Lebih banyak kajian dengan saiz pesakit yang lebih besar diperlukan untuk mengkaji kesan premedikasi *midazolam* secara oral dalam DGA pediatrik untuk mengetahui kesan maksima premedikasi.

CHILDRENS' BEHAVIOUR AND PHYSIOLOGICAL PARAMETERS AT RECOVERY FOLLOWING DENTAL GENERAL ANAESTHESIA WITH AND WITHOUT PREMEDICATION ORAL MIDAZOLAM AT HOSPITAL UNIVERSITI SAINS MALAYSIA: A PRELIMINARY STUDY

ABSTRACT

Oral midazolam premedication usually prescribed for controlling behaviour and reducing anxiety of children and the use under general anaesthesia (DGA) on the behavioural and physiological status of uncooperative paediatric patients have not yet been well explored. This study is aimed to evaluate the effect of oral midazolam premedication on recovery behaviour and physiologic parameters of children undergoing DGA. Thirty uncooperative children aged from 2–11 years were involved in this randomised control trial study. Group I: Received 0.5 mg/kg midazolam orally 30 minutes before entering the operation theatre, while Group II: Did not receive any premedication. Their physiologic parameters were measured at the post anaesthesia care unit (PACU). The recovery behaviour was also recorded for the evaluation using the Modified Houpt Behavior Rating Scale. There was no significant differences in all recovery behaviour and physiologic parameters for both groups ($p>0.05$). No significant association of premedication oral midazolam with successful recovery behaviour ($p=0.381$). However, an interesting trend of positive recovery behaviour and physiology was observed among children with oral midazolam premedication. More studies with larger sample size are needed to explore the effect of oral midazolam in paediatric DGA as to discover the optimum effect of premedication.

CHAPTER 1

INTRODUCTION

Even after years of professional experience, many dental professionals find that managing uncooperative or anxious children is a remarkable challenge. It is somewhat a different management required in dealing with children when compared to adult patients. Children may show various favourable behaviours during dental visits and dental treatment, such as compliance with command, keep still during treatment, listen attentively and interact effectively. Meanwhile, others may become uncontrolled and unfavourable to deliver dental treatment in chairside.

1.1 Dental Anxiety and Behaviour of Paediatric Patient

Dental anxiety and unfavourable behaviour are two major and common problems in managing uncooperative paediatric patients (Klingberg, 2008). It is known to be associated with several factors such as dental pain, negative previous dental experiences, and young age (McNeil *et al.*, 2011; Ramos-Jorge *et al.*, 2006; Weiner, 1990). In Malaysia, a study reported that preschool children had high dental anxiety (Esa *et al.*, 2020). Similar results were shown among children from other parts of the world, reporting high dental anxiety between 8.9% and 20.6% (Kilinc *et al.*, 2016; Lee *et al.*, 2007; Nakai *et al.*, 2005; Yamada *et al.*, 2002). The highly anxious children have a tendency to practice irregular dental visits and dental care avoidance (Eitner *et al.*, 2006; Locker, 2003). Children could experience preoperative anxiety or fear and be unable to fully cooperate with the dentist.

As for treatment under general anaesthesia (GA), this anxiety if left untreated may lead to difficulty in mask induction, increase in postoperative pain, emergence delirium, psychological effects after treatment and behavioural problems during procedure in the operation theatre (Mehrotra, 2019).

1.1.1 Factors Affecting Dental Anxiety in Children

Children's behaviour when receiving treatment is influenced by several factors (Alasmari *et al.*, 2018). The child's age is nearly universally acknowledged in the literature as a predictor of behaviour during dental treatment. For instance, younger children are more likely to experience dental anxiety compared to older children. Another important factor is the child's gender. Contradicting findings have been reported in the literature regarding dental anxiety in male and female children. Nevertheless, most studies acknowledged that girls experienced more dental anxiety when compared to the opposite gender (Alasmari *et al.*, 2018).

Previous dental and medical treatments may influence dental anxiety. When children visit the dentist for the first time, they often experience high levels of dental anxiety. Children who had unpleasant medical experiences and were exposed to invasive medical treatments were observed to be more fearful of dental procedures (Hollis *et al.*, 2015). Notably, DGA is one of the invasive treatments in a child patient, thus may be involved in his or her crucial childhood emotional milestone. Children may be traumatised as a result of the severe anaesthesia induction process and experience most postoperative adverse effects of treatment under GA like pain, headache, bleeding from extraction sites and others (Hosey *et al.*, 2006).

1.2 Behaviour Management of Uncooperative Children

In paediatric dentistry, managing the patient's behaviour is the mainstay of the success for each dental treatment. The main goals of behaviour management, according to the American Association of Pediatric Dentistry (AAPD), are to: : 1) To establish communication with children, 2) To alleviate the child's dental fear and anxiety in dental setting, 3) To promote patient's and parents' awareness of the need for good oral health and the process by which it is achieved, 4) promote the child's positive attitude toward oral health care, 5) build a trusting relationship between dentist/staff and child/parent, and 6) provide quality oral health care in a comfortable, minimally- restrictive, safe, and effective manner (AAPD, 2022).

Children's behaviour can be managed via several techniques either non-pharmacologic or pharmacological intervention. The choice of approach or intervention depends on the operator's assessment of the child's current behaviour and response. To date, there is no golden approach above others stated in current guidelines, and in most cases, it can either be applied interchangeably or in combination of approaches.

1.2.1 Non-Pharmacological Approach of Behaviour Management

This management involves no drug intervention, and focuses more on the patient's emotional and behaviour shaping strategies. Several guidelines have been developed to assist dental professionals in the use of non-pharmacological behaviour management measures among children (Campbell *et al.*, 2011; Roberts *et al.*, 2010). No single strategy can be performed in every case, thus combined management procedures are frequently used (Campbell *et al.*, 2011).

An appreciation of the connection of a child's age, their cognitive development, personality trait and dental anxiety facilitates the selection and application of non-pharmacological behaviour management strategies (Lewis, 2020). The British Society of Paediatric Dentistry (BSPD) (Campbell *et al.*, 2011) and the European Academy of Paediatric Dentistry (EAPD) (Roberts *et al.*, 2010) have both recommended basic non-pharmacological behaviour management strategies as depicted in Table 1.1.

Table 1. 1 Non-pharmacological behaviour management strategies

Recommended Strategy	Definition/Examples
Providing preparatory information	Pre-appointment letters, including a description of what to expect during the appointment.
Verbal communication	Avoiding negative or emotive language, choose child-friendly and age-appropriate words.
Non-verbal communication	Gentle pats or squeezes to relieve distress, child-friendly setting, friendly and smiling dental team
Voice control	Altering volume, tone and pace as necessary.
Tell-Show-Do	Tell: age appropriate explanation e.g. slow handpiece as a 'digger'. Show: demonstration e.g. shown vibrations on finger. Do: without delay.
Enhancing control	Using a stop sign or hand-signalling/stop signal (green, amber, red dependent on level of discomfort).
Positive reinforcement	Selective reinforcement of specific positive behaviours, increasing the probability of repetition of the ideal behaviour e.g. "You are getting a sticker/badge for opening really wide". Negative reinforcement has been shown to be less effective.
Modelling	Learning through observation of others in person or on video, with a favourable consequence at the end of the visit.
Distraction	To help with more unpleasant operations, divert the child's attention to something else, such as cartoons, audio, urging the child to clench their fist to prevent gagging, or tugging on their lip while giving local anaesthesia.
Systematic desensitisation	Relaxation, then exposure to fear-producing stimuli in a hierarchical order (from least to most terrifying), only progressing when the patient feels ready.

The American guideline recommended basic behaviour guidance in managing paediatric children; i) Communication and communicative guidance, ii) Positive pre-visit imagery, iii) Direct observation, iv) Tell-show-do, v) Ask-tell-ask, vi) Voice control nonverbal communication, vii) Positive reinforcement and descriptive praise, vii) Distraction, ix) Memory restructuring, x) Desensitisation to dental setting and procedures, xi) Enhancing control, xii) Communication technique for parents (and age-appropriate patients), xiii) Parental presence/absence, xiv) Sensory-adapted dental environments (SADE), xv) Animal-assisted therapy (AAT), and xvi) Picture exchange communication system (PECS) (AAPD, 2020).

1.2.2 Pharmacological Approach of Behaviour Management

When non-pharmacological strategies for managing behavior are ineffective, the pharmacological method can be employed to reduce dental fear and anxiety in children, promoting a state of calmness and relaxation. This method involves the administration of different drugs or medications to regulate the behavior of pediatric patients during dental procedures. The pharmacological approach can be classified into two distinct categories (Shafi *et al.*, 2020):

a) Sedation, which further includes; minimal sedation (anxiolysis), moderate sedation (conscious sedation) and deep sedation

b) General anaesthesia

1.3 Dental General Anaesthesia (DGA) in Paediatric Patient

GA is defined as "a controlled state of drug-induced loss of consciousness in which patients cannot be awakened even by painful stimuli and lose their defensive reflexes" (American Society of Anaesthesiologists, 2014; Bailey *et al.*, 2019) . In many cases of GA, independent ventilatory performance is insufficient and cardiovascular function may be compromised (American Society of Anesthesiologists, 2014). Thus, the decision of choosing the DGA must be considered by the dentist after thorough assessment based on the interplay of fundamental factors.

According to Oubenyahya and Bouhabba (2019), the following factors should be considered by the dental professional and the child's caregiver before deciding to employ DGA;

a) The degree of non-cooperation of the child due to a lack of psychological or emotional maturity and/or mental, physical, or medical disability.

b) The degree of anxiety exhibited, which can lead to an uncommunicative child.

c) The presence of complex medical conditions.

d) The very young age of the patient, which might contraindicate the use of other sedation strategies in the anaesthesia continuum.

e) The failure of other behavioural guidance modalities.

f) The duration of the intervention and need for immediate pain relief or significant surgical procedures.

g) The presence of allergies that absolutely contraindicates local anaesthesia, the presence of an acute infection, or anatomic variations that render local anaesthesia ineffective.

Children who are undergoing GA should be monitored before undergoing elective or emergency surgery. Fasting guidelines must be followed for healthy children who undergo elective surgery, according to the American Society of Anaesthesiologists (ASA) Committee on Standards and Practice Parameters (American Society of Anaesthesiologists Committee, 2011);

a) Staying hydrated for at least 2 hours before anaesthesia. For a child aged 12 and up, you may give 3 mls/kg up to a maximum of 200 mls.
b) Breast milk – the last feed should occur four hours prior to anaesthesia.
c) Formula milk and a meal should be consumed at least 6 hours prior to anaesthesia.
d) Intravenous fluids should be started as soon as possible to help you get through the fasting period.
e) If there is a list, consult with the anaesthetist in charge because the timing and order of the list may change.

1.3.1 The Use of Dental General Anaesthesia for Children in Malaysia

The need for DGA among paediatric patients is increasing by year (Karim *et al.*, 2008). Between 2003 and 2007, 349 children received dental treatment under GA, with 43.6% and 34.4% with medical and behavioural issues, respectively (Karim *et al.*, 2008). Another study in Selangor reported that the majority of children aged two to six who were diagnosed with early childhood caries had undergone dental treatment under GA, with extractions being the most common therapy, followed by restorations (Hashim *et al.*, 2019).

A recent study conducted in Hospital Universiti Sains Malaysia (Hospital USM) reported the number of cases has risen over time, eventually reaching 104 cases in 2018 (Samsudin *et al.*, 2021). The most common diagnosis was early childhood caries (ECC) with 188 cases (53.1%), followed by dental caries (25.1%) and dentoalveolar abscess (17.5) (Samsudin *et al.*, 2021).

1.3.2 Indications of Dental General Anaesthesia

DGA is indicated after all the less invasive behaviour management deemed not justifiable on some patients. For example, GA may be required if dental treatment in the primary dental care setting using local anaesthesia has been previously unsuccessful. In the presence of acute orofacial infection, the use of local anaesthesia might be ineffective or contraindicated. Thus, DGA may be indicated for paediatric patients. Sometimes, children require dental extraction in multiple quadrants, and DGA may be performed as one of treatment options. It is also utilised for the complex dental procedure such as surgical removal of impacted teeth, management of orofacial fracture and repair of cleft lip and palate. DGA is also needed for uncooperative paediatric patients due to young age (less than 4-year-old) and those having physical and/or mental disabilities or medically-compromised patients (Adewale, 2012).

DGA is frequently indicated for children who have dental fear, dental anxiety, or are physically resistant to receiving dental treatment after a few unsuccessful chairside dental management attempts. It is crucial to maintain the development psychology of those children who are reluctant or uncooperative while also minimising medical risk and complications (Sharma *et al.*, 2015).

1.3.3 Contraindication of Dental General Anaesthesia

An evaluation is performed before the GA procedure, which includes a brief history and documenting any clinical concerns (Little *et al.*, 2017; Bailey *et al*., 2019). Drug sensitivities, medical history, and past reactions to sedatives are all crucial elements to be recorded (Bailey *et al.*, 2019). Any entanglements discovered in children who have previously received GA are critical in extending the demonstrated ailment prior to surgery (Smith *et al.*, 2020). With the exception of parental refusal, there are currently no absolute contraindications to GA in children. In any case, there are a few relative contraindications to using this system, such as illnesses that have not improved prior to an elective medical procedure, children with a difficult aviation route, or other critical comorbidities like severe aortic stenosis, severe pneumonic illness, or congestive cardiovascular breakdown.

1.3.4 Effects of Dental General Anaesthesia

The goals of DGA include improving the quality of life for young patients, special needs patients, and those with dental phobia or anxiety, and instilling positive attitudes in parents and children on oral health (Sharma *et al.*, 2015). Nevertheless, similar to other treatments under GA, DGA imposes effects or risks to a child patient. The risk of GA varies depending on the age of the child, the presence of various diseases, and the type of surgery (Zhang *et al.*, 2020). Memories and experience are vital in children's developmental growth as to assist in performing new imagination or thinking processes. Short term memories tend to be impaired in patients under GA with propofol than sevoflurane, which lasts within seven days postoperative, and then recovered to baseline levels at three months following GA (Yin *et al*, 2014).

Breathing problems, sporadic pulses, an unfavourably susceptible response to medications, a delay in the arrival of a typical memory work, cerebrum harm, or even death in rare cases are just a few of the disadvantages of GA (Khodadadi *et al.*, 2018).

1.3.5 Recovery Behaviour of Dental General Anaesthesia

Each case that involves operative procedure needs to undergo a recovery surgery phase post-operatively. This phase includes close observation at the post recovery area in the operation theatre setting. Children display a wide range of post-operative or recovery behaviour when undergoing general anaesthesia procedure. The distress behaviour such as crying, verbal pain, verbal resistance and non-verbal support request were reported to be positively associated with the analgesic used during GA and post-operative pain scores (Chorney *et al.*, 2012). Significant psychological effects may result from the prolonged hospitalisation and/or GA experience (Zainal Abidin *et al.*, 2021). Parental presence made no difference in decreased crying and negative behaviour change post-operatively at the recovery room, and this finding was reflected significantly in children less than five years of age (Lardner *et al.*, 2010). Many behaviour assessment tools have been applied to measure a patient's recovery behaviour, particularly based on an operator's observation (Baygin *et al.*, 2016; Chorney *et al.*, 2012).

The information regarding children's recovery behaviour is crucial for further exploration of associated factors mainly in terms of managing preoperative behaviour, as this may affect their future acceptance towards dental treatment. The postoperative period is the most critical time in an individual life. Each element of postoperative maladaptive behaviours, preoperative anxiety, and emerging delirium in children has an interchangeable relationship and confounding effects (Zainal Abidin *et al*., 2021).

The term “emergence delirium” (ED) is used widely in paediatric anaesthesia. It can be defined as “a disturbance in a child’s awareness of and attention to his/her environment with disorientation and perceptual alterations including hypersensitivity to stimuli and hyperactive motor behaviour in the immediate post anaesthesia period” (Sikich & Lerman, 2004). ED appears from the second extubation of GA performed and may last up to 30 minutes or two days.

As the patient leaves the operation theatre, an intent observation care needs to be conducted to ensure the patient's life is guarded towards survival. Several factors influence postoperative complication of children undergoing general anaesthesia that must be considered such as age, type of anaesthetic used during induction, duration of anaesthesia, type of procedures and pre-operative conditions (Jaensson *et al.*, 2018).

1.3.6 Recovery Physiology Parameters of Dental General Anaesthesia

The recovery physiology is the post-operative observation that includes the physiological parameters of anaesthetic and treatment under GA, particularly the patient's vital signs. There are several components in vital signs that are common for close observation postoperatively, such as room air oxygen saturation level, heart rate, respiratory rate, blood pressure and body temperature (Coté & Wilson, 2019). The neurotransmitters, gamma-aminobutyric acid (GABA) and glutamate, and their corresponding receptors primarily enhance natural death of some neurons during the rapid proliferation phase (apoptosis) and synaptogenesis (Loepke & Soriano, 2008).

When benzodiazepines, barbiturates, chloral hydrate, propofol, and ketamine interact with the receptors, concerns are raised about increased apoptosis and potentially harmful long-term neurodevelopment effects (Loepke & Soriano, 2008).

In infants and young children, recent studies found no significant longer-term neurodevelopmental effects when compared to unexposed populations in short GA exposure of less than 90 minutes (McCann *et al.*, 2019; Warner *et al.*, 2018; Sun *et al.*, 2016).

The values and normal ranges for respiratory rate (RR) and heart rate (HR) in children are presented in Table 1.2. While Table 1.3 depicts a normal range of pulse oxygen saturation according to the American College of Critical Care Medicine (Crone *et al.*, 1989).

Table 1.2 The values and normal ranges for respiratory rate (RR) and heart rate (HR) in children

Normal ranges for respiratory rate (RR) and heart rate (HR) in children				
Age	**Guide weight (kg)**		**RR at rest**	**HR**
	Boy	**Girl**	**(breath per minute)**	**(beats per minute)**
At Birth	3.5	3.5	25-50	120-170
1 month	4.5	4.5		
3 months	6.5	6	25-45	115-160
6 months	8	7	20-40	110-160
12 months	9.5	9		
18 months	11	10	20-35	100-155
2 years	12	12	20-30	100-150
3 years	14	14		90-140
4 years	16	16		80-135
5 years	18	18		
6 years	21	20		80-130
7 years	23	22		
8 years	25	25	15-25	70-120
9 years	28	28		
10 years	31	32		

*Adapted from Paediatric Protocols For Malaysian Hospitals 4th Edition, 2019

Table 1.3 Vital signs of Pediatric Advanced Life Support according to The American College of Critical Care Medicine

Variable	Units	Neonate	6 months	12 months	3 years	5 years	9 years	12 years
Pulse oxygen saturation	mmHg	60-90				80-100		

*Adapted from O'Rourke and Crone . O'Rourke PP, Crone RK. The respiratory system. In: Gregory GA, editor. Gregory's pediatric anaesthesia. 2nd ed. New York: Churchill Livingstone; 1989. p. 63–91.

1.4 Premedication in Children

Children who are put under GA may experience fear and anxiety. When children are in an unfamiliar environment with unknown people, they become more nervous and fearful. Premedication is the use of drugs prior to GA to reduce anxiety thus assisted in the anaesthesia intubation process. Morphine was the first drug to be used in 1850 by Turin and Nussbaun between 1829 and 1890 to reduce the amount of anaesthetic required (Gregory, 1994).

Even though the use of premedication prior GA is not a routine practice nowadays, it is constantly evolving, with more research on premedication drugs (Sheen *et al.*, 2014). The following are the objectives of premedication prior GA in general (Gregory, 1994):

a) To induce drowsiness, anxiety relief, and trauma relief.

b) To eliminate unwanted autonomic reflexes (vagal).

c) To reduce the volume and acidity of the contents of the stomach.

d) To improve the efficiency and safety of anaesthesia induction.

e) To bring about amnesia.

f) Combine with anaesthesia to reduce the need for GA medications.

g) To prevent post-surgery nausea and vomiting.

Barbiturates, narcotics, benzodiazepines, butyrophenones, antihistamines, anticholinergics, H2 receptor antagonists, antacids, and other drugs are used as premedication. The following characteristics should be present in an ideal premedication (Phaltankar & Shah, 2017);

a) A pleasant and secure method of administration.

b) A prompt and steady commencement.

c) Few negative consequences and rapid elimination.

Children's premedication can be given orally, intramuscularly, intravenously, rectally, sublingually, or intranasally. Oral premedication minimises the pain of injecting a child with a needle but its advantages include a slower onset and lower bioavailability of the premedication agents (Phaltankar & Shah, 2017). The following patient's characteristics determined the type and dosage of the premedication (Phaltankar & Shah, 2017) :

a) The age and weight of the patient.

b) Physical condition.

c) Anxiety level of the patient.

d) Tolerance to antidepressants.

e) Adverse reactions to premedication drugs in the past.

f) Surgical procedure (either elective or emergency).

g) Surgical inpatient or outpatient.

Premedication with drugs like phenothiazines, benzodiazepines, opioid analgesics, and barbiturates has been used in paediatric patients through a variety of routes. Table 1.4 depicts the different types of sedative drugs.

Table 1. 4 Different types of sedative drugs

Type of drugs	Route of administration and dosage	Indication	Special consideration
Midazolam	a) Intravenous 0.1mg/kg b) Oral 0.4-0.5mg/kg (max 15mg) c) Intranasal 0.2-0.3mg/kg d) Rectal 0.3-0.5mg/kg (max 15mg)	Minimal sedation	Paradoxical CNS stimulant
Propofol	a) Intravenous 1-2 mg/kg iv b) Target Controlled Infusion (TCI) 0.5-2mcg/ml c) Infusion 6-10mg/kg/hour	Moderate or deep sedation	Injection pain, apnoea
Ketamine	a) Intravenous 0.5-2 mg/kg iv bolus then 0.25-1 mg/kg prn b) Intranasal 2-4 mg/kg	Dissociative sedation and analgesia	Combination with midazolam or propofol for reduction of psychomimetic side effects
Clonidine	a) Intravenous or Intranasal 1-2mcg/kg b) Oral 2-3mcg/kg	Anxiolysis	Slow onset
Dexmedetomidine	a) Infusion 0.2-0.7 µg/kg/hr b) Oral or Intranasal or Buccal 2-3 µg/kg	Moderate and deep sedation, small analgesic effect	Slow onset, spontaneous respiration

Table 1. 4 Continued

Type of drugs	Route of administration and dosage	Indication	Special consideration
Remifentanil	a) Infusion 0.1-0.3 μg/kg/min	Analgesia	Apnoea
Fentanyl	a) Intravenous 1-2 μg/kg	Analgesia	Apnoea

*Adapted from Malaysia Society of Paediatric Anaesthesiologists (MSPA), *Paediatric Anaesthesia Handbook*. Malaysia. (pp. 36)

Despite the widespread availability and use of a wide range of premedication, no universal agreement exists on the best premedication and route of administration for children (Phaltankar & Shah, 2017).

1.4.1 Midazolam Premedication

Given its rapid onset of action and short elimination half-life, midazolam is commonly used as a premedication in paediatric patients via various administration routes (Phaltankar & Shah, 2017).

1.4.2 Pharmacology of Midazolam Premedication

Benzodiazepines were first introduced as sedative-hypnotic and anxiolytic agents, and now employed as a common anaesthetic medication. Midazolam is a water-soluble imidazobenzodiazepine derivative and the most commonly used sedative premedication in paediatric patients (Jain *et al.*, 2020; Phaltankar & Shah, 2017). The chemical structure of Midazolam can be gleaned from its chemical name: 8-Chloro-6 (2-fluorophenyl)-1-methyl-4H-imidazo (1,5-a) (1,4)-benzodiazepine (Phaltankar & Shah, 2017). The imidazole ring is relatively basic, so it can be used to prepare salts that are stable in aqueous solution (Phaltankar & Shah, 2017).

A portion of the medication in the solution has an open benzene ring at pH levels below 4, which makes it water soluble. The lipid solubility of all of the drugs is increased because they are present in the 'ring close to' at a physiological pH (Phaltankar & Shah, 2017).

1.5 Problem Statement

Children respond unpredictably towards planned or ongoing dental treatment. Management of dental treatment under GA is commonly required for pre-cooperative children with complex dental problems, apart from those that are medically compromised or with special needs. Therefore, further intervention and supplementation need to be performed in managing and reducing dental anxiety of children, especially those who are classified as severely anxious. One of the solutions is the use of premedication to manage this problem. To date, there is no consensus in using premedication preoperative, particularly in paediatric DGA.

Undoubtedly, there are many arguments on the amnestic effects that may result in paediatric patients displaying more distressed behaviours in the intermediate post-operative duration (Stewart *et al.*, 2006). A study reported that midazolam has no anxiolytic effect on impetuous children (Finley *et al.*, 2006). Results from a previous study revealed that midazolam is widely used as premedication sedation, but it's recovery behaviour and physiology effects in paediatric dental treatment are still not understood (Finley *et al.*, 2006). These findings reflect the use of oral midazolam (OM) as premedication sedation in children requires further investigation in monitoring behaviour of children post-operatively. Hence, this study was aimed to assess postoperative recovery behavioural and physiological parameters of oral midazolam as sedative premedication in paediatric patients requiring dental treatment under GA.

1.6 Justification of the Study

The initial purpose of premedication prior to GA is to counter the adverse effects of anaesthesia. Currently, the aims are more focused on the efficacy of premedication in improving patients' general well-being and satisfaction post-operatively. Nevertheless, many patients still encounter low quality of recovery from GA, while others are not treated adequately. In children, the traumatic experience prior, during or post GA should be limited to avoid the unpleasant developmental towards healthcare, including the dental treatment. To date, the use of premedication is not a routine practice in any of the available guidelines. Multiple factors need to be explored further in terms of the safety, efficacy, indications of premedication.

Generally, there is a vague corroboration and understanding of the post-operative and other relevant effects of premedication involving midazolam. Most studies on premedication OM in GA have focused on medical procedures, whereas DGA has only been studied in a few cases. Furthermore, it is known that many factors influence the recovery behaviour and physiology parameters post-GA. Apart from the patient's preoperative behaviour, other factors are also vital including traumatic experience pre-operative time, anaesthetic drugs used, patient's age and gender, duration of surgery and post-operative pain. The use of premedication is part of assistance in reducing the pre-operative distress particularly in children, hence its association with recovery behaviour and effect on physiological parameters during post-operative recovery monitoring is still in doubt.

1.7 Conceptual Framework of the Study

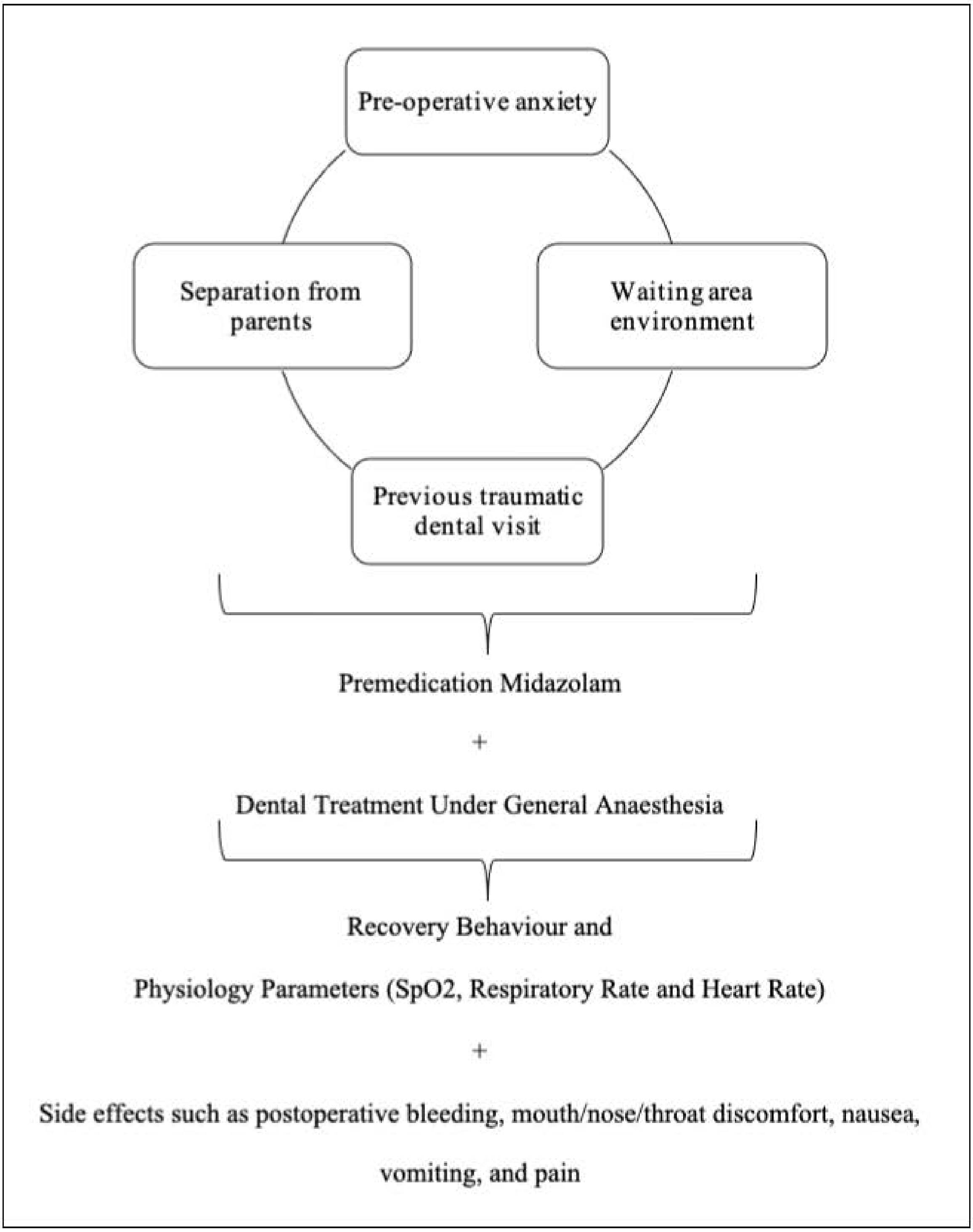

Figure 1.1 Conceptual Framework of Behaviour Recovery of Children

1.8 Objectives

1.8.1 General Objective

To evaluate recovery behaviour and physiology parameters of children undergoing dental general anaesthesia with or without premedication oral midazolam at Hospital Universiti Sains Malaysia (Hospital USM), Kubang Kerian, Kelantan.

1.8.2 Specific Objectives

1. To determine the recovery behaviour score in children with and without premedication oral midazolam (OM) for DGA.
2. To determine the physiology parameters of post-DGA in children with and without premedication OM includes oxygen saturation (SpO_2), respiratory rate and heart rate.
3. To assess the recovery behaviour of post-DGA in children with premedication OM to those without premedication OM.
4. To compare the physiology parameters of post-DGA in children with premedication OM to those without premedication OM.
5. To determine the association of premedication oral midazolam with positive recovery behaviour.

1.9 Research Questions

1. What is the recovery behaviour scale among children with and without taking premedication oral midazolam for DGA?
2. What are the post-operative physiology parameters of children with and without taking premedication oral midazolam for DGA?
3. Is there any difference in post-operative recovery behaviour among those children who take premedication oral midazolam with those otherwise?
4. Is there any difference in post-operative physiology parameters among those children who with or without premedication oral midazolam?
5. Is there any association of premedication oral midazolam with positive recovery behaviour?

1.10 NULL Hypotheses

1. There is no significant difference in post-operative recovery behaviour and physiology parameters among those children with and without premedication oral midazolam.
2. There is no association of premedication oral midazolam with positive recovery behaviour.

CHAPTER 2

LITERATURE REVIEW

2.1 Dental General Anaesthesia (DGA)

General anaesthesia is a drug-induced loss of consciousness in which patients are not aware even by painful stimulation (Coté & Wilson, 2019). Uncooperative children who are healthy or medically stable individuals (ASA I, II) may be considered for the use of deep sedation or GA in dental treatment. Clinical guidelines and information for GA are mentioned in "Guidelines for the Use of Sedation and General Anesthesia by Dentists" (American Dental Association, 2016). Those readily anxious children who are indicated for DGA are eligible to experience recalling moments in the OT room that begins with the anaesthesia mask placement, followed by the unpleasant smell of the sevoflurane in oxygen gases (Baygin *et al.*, 2016).

DGA is frequently used as a treatment option to manage uncooperative patients (Savanheimo *et al.*, 2012). In New Zealand, a 65% increase in the number of children receiving dental treatment under GA was recorded between 2004 and 2014 (Hunt *et al.*, 2018). Furthermore, many other European, Asian, and Middle-east countries have expanded the use of DGA (Cantekin *et al.*, 2014). In Malaysia, the number of children who underwent DGA increased by 200% between 2015 and 2016 (Samsudin *et al.*, 2021). In 2017, the number of children undergoing DGA remained constant while in 2018, the number of instances rode steadily and eventually amounted to 104 cases (Samsudin *et al.*, 2021). AAPD in their guideline suggested the use of GA for those having a physical or medical disability, and patients who are extremely fearful, anxious or not communicating (AAPD, 2005).

It has been estimated that 9.6% of all paediatric patients seen in dental clinics were indicated for dental treatment under GA, with the majority between 3 and 6 years of age (Campbell *et al.*, 2018). Meanwhile, about 349 children in Malaysia who underwent dental GA, 56.4% of them had no known medical illness as they were either indicated for complex dental treatment, high dental anxiety or combination of both (Karim *et al.*, 2008). As for dental treatment, 97.8% and 2.2% of deciduous and permanent teeth were extracted, respectively (Karim *et al.*, 2008). On the other hand, 75.7% of deciduous and 24.3% of permanent teeth were restored while 24.1% involved surgical treatment (Karim *et al.*, 2008). In Kuwait, behaviour problems in healthy patients and those with special needs were the common admission for dental procedures under GA (Ibricevic *et al.*, 2001).

The effects of GA can be viewed and described as side effects or complexities. Queasiness, retching, migraine, dazedness, sluggishness, shuddering, sore throat, agony, and disturbance are some of the side effects of sedative medications or medicines (Zhang *et al.*, 2020). During laryngoscopy and endotracheal intubation, wounds to teeth, lips, and other delicate tissues have been reported, as well as the use of mouth openers incorrectly or excessively during a technique (Ramazani, 2016). The other common postoperative complications include bleeding, problem in eating, mouth/nose/throat discomfort, nausea-vomiting, constipation, fever and others (Cantekin *et al.*, 2014). Several outcomes of DGA have been highlighted, with postoperative quality of life as the main focus. A study reported improved quality of life in children who received dental treatment under GA, characterised by a reduction of 44% in total Early Childhood Oral Health Impact Scale (ECOHIS) scores (Cantekin *et al.*, 2014).

A similar result was highlighted in a study involving 120 parents/caregivers of preschool children receiving dental treatment under GA with a reduction of 54.7% in total ECOHIS scores after treatment (Almaz *et al.*, 2019). A meta-analysis found that the Child Oral Health-Related Quality of Life (COHRQoL) improved in children who received dental treatment under GA collectively (Park *et al.*, 2018). The latter report also reflected a 27.6% to 91% reduction in the ECOHIS score with a median ranging from 0.71 to 2.49. Needleman *et al.* (2008) documented moderate intensity of postoperative pain and the highest was observed immediately postoperatively in 95% of the 90 children who underwent dental rehabilitation under GA (Needleman *et al.*, 2008). A significant postoperative discomfort, specifically regarding nasotracheal intubation, in 59% of children undergoing DGA (Cantekin *et al.*, 2014). Approximately 52% of children demonstrated negative behaviour changes on day 1 postoperatively (Beringer *et al.*, 2014).

However, there are limited reports on patients' behaviour focusing on the moment the patient arrives at the recovery room and within the close observation postoperatively.

2.2 Midazolam as a Premedication Sedation Drug

Benzodiazepine was introduced as sedative-hypnotic and anxiolytic agents and commonly used medication in anaesthesia practice. Midazolam is an imidazobenzodiazepine derivative and water-soluble benzodiazepine and the most commonly used sedative premedication in paediatric patients (Phaltankar & Shah, 2017; Jain *et al.*, 2020). Direct activation of gamma-aminobutyric acid (GABA) interacts with inhibitory neurotransmitter receptors and exerts the effects of Midazolam.