Effect of caregiver's recorded voice on emergence delirium in children undergoing dental surgery

Marisha Bhagowat

A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg in partial fulfilment of the requirements for the degree of Master of Medicine in the branch of Anaesthesiology.

Johannesburg, 2020

Declaration

I, Marisha Bhagowat declare that this research report is my own unaided work. It is being submitted for the Degree of Master of Medicine in the branch of Anaesthesiology at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.

Signature

23 October 2020

Abstract

Background

Emergence delirium (ED) is a distressing and harmful postoperative complication following general anaesthesia. The aim of this study was to compare the incidence of ED in children listening to either a recording of their caregiver's voice or a stranger's voice, during emergence from general anaesthesia for elective dental surgery, at Rahima Moosa Mother and Child Hospital.

Methods

A prospective, randomised and contextual study design was implemented with convenience sampling. This study included children between 2 – 6 years of age who were randomly assigned to caregiver voice group (Group C) or stranger voice group (Group S).

Results

The ED incidence within the total sample was 11 (16.9%). In Group S, 4 (15.4%) children had ED, whereas in Group C, 7 (25%) children had ED (p=0.475). There was no significant difference in Pediatric Anesthesia Emergence Delirium (PAED) scale and the Face, Legs, Activity, Cry and Consolability (FLACC) scores between the two groups. The time from completion of surgery to first purposeful movement and to tracheal extubation was similar in Groups C and S (p=0.595, p=0.992 respectively). ED management and duration in the recovery room were also similar (p=0.300, p=0.326 respectively). There was an overall strong positive correlation between highest FLACC and highest PAED scale scores (r=0.827, p<0 .0001).

Conclusion

The PAED scale scores and the ED incidence were similar in children who listened to either a recording of their caregiver's voice or a stranger's voice.

Acknowledgements

I would like to thank my supervisors Juan Scribante, Helen Perrie and Thomas Kleyenstuber for their guidance and patience.

I am also grateful to the Department of Anaesthesiology at Rahima Moosa Mother and Child Hospital for their enthusiastic participation.

I am also thankful to my family, especially to my sister Alisha, for their unfaltering support.

Table of contents

List of figures

List of tables

Abbreviations

ASA	American Society of Anesthesiologists Classification
CNS	Central nervous system
EEG	Electroencephalogram
ED	Emergence delirium
FLACC score	Faces, Legs, Crying, Consolability score
Group S	Stranger voice group
Group C	Caregiver voice group
LMA	Laryngeal mask airway
LC	Locus coeruleus
MRI	Magnetic Resonance Imaging
mYPAS	modified Yale Preoperative Anxiety Scale
NPM	Non-pharmacological management
PAED scale	Paediatric Assessment of Emergence delirium scale
PMB	Post-operative maladaptive behaviour
PMS	Proton Magnetic Resonance Spectroscopy
RMMCH	Rahima Moosa Mother and Child Hospital
RA	Research assistant
TIVA	Total intravenous anaesthesia

Statement

The Research Report consists of a literature review, draft article, study proposal and appendices. The study proposal is included for background reference and is not for examination.

The formatting of this Research Report complies with the University of the Witwatersrand's Style Guide for Theses, Dissertations and Research Reports. The formatting of the draft article may differ from the author guidelines stipulated by the South African Journal of Anaesthesia and Analgesia, the journal to which it is intended to be submitted, in order to comply with the university's style guide.

Section 1: Review of the literature

1.1 Introduction

This literature review will commence with a brief history of emergence delirium (ED). It will then follow with the definition and incidence, outcomes and complications. Thereafter, ED risk factors, physiology and measurement tools will be considered. Lastly, the preventative and treatment strategies of ED will be described.

1.2 History of emergence delirium

In 1940 Arthur Guedel reported one of the earliest findings of ED.

> Emergence delirium is greater and more active with cyclopropane than with any other anesthetic agent … In the past two years we have been adding ether during the latter part of the surgery with the idea of lessening muscle activity and slowing of emergence, and this has been our most successful – or should I say least unsuccessful – protection against this phenomenon (1).

Two decades later in 1960 Smessaert et al (2) conducted one of the first ED studies. The study included participants older than 10 years who were categorized into the following modes. Mode 1 were participants who had a tranquil emergence. Mode 2 were participants who had a moderately agitated emergence. Mode 3 were those who were extremely uncooperative and had a severely agitated emergence. Seventy six percent displayed a tranquil emergence, 20% a moderate agitation, and 3% extreme delirium, with the highest incidence among adolescents and teenagers. The study further identified the associative relationships between ED and psychological characteristics, such as anxiety, and specific anaesthetic agents, such as cyclopropane. It also established the relationship between ED and the operative site: thoracic and abdominal surgery were associated with the highest ED incidence (2).

In 1961 Eckenhoff et al (3) conducted an ED study that included both infant and geriatric patients. The study reported an inverse relationship between ED and age. Among the 14 436 patients, the highest ED incidence was found within the 3 – 9 year age group. Furthermore, the study identified the inverse relationship between ED and the patient's

American Society of Anesthesiologists Classification (ASA) of physical status. ASA I patients had the highest ED incidence, whereas ASA 4 and 5 demonstrated no features of ED (3).

1.3 Definition and incidence of emergence delirium

ED is an altered state of consciousness. It is a transitory period that begins from the cessation of anaesthesia and ends with the return of complete consciousness, it is self-limiting and usually resolves within 45 minutes (4). During this period children are inconsolable and unresponsive to even their caregivers, exhibit non-purposeful movement and their eyes characteristically avert, stare or are closed (5).

Emergence agitation is the umbrella term that includes ED and agitation during emergence from anaesthesia secondary to pain, hypotension, hypocarbia, hypercapnia, increased intracranial pressure, hypothermia (6), hypoxia and hypoglycaemia (6, 7). Emergence agitation thus encompasses the differential diagnosis for ED, and highlights that an ED diagnosis is one of exclusion.

Eckenhoff et al (3) reported that the general incidence of ED is 5.3%, with ED almost three times more common in children than in adults. The paediatric ED incidence ranges from 10 – 60% (4, 8-15) but has been reported to be as high as 80% (13). This wide range in ED incidence may be attributed to the inconsistency in utilised ED measurement scales, varying study designs and protocols and pain further confounding the diagnosis of ED.

1.4 Measurement tools of emergence delirium

A variety of measurement tools have emerged such as the Pediatric Anesthesia Emergence Delirium (PAED) scale (16), the Watcha (17) and Cravero (13) scores. The three scales have been shown to correlate well with one another in ED diagnosis (18). Despite the PAED scale being clinically cumbersome, it has been validated with internal consistency and reliability, resulting in its common use in ED literature (16, 19). In the PAED scale, the scores for each of the five psychometric items are added to achieve a total score out of 20. A score ≥10 has 64% sensitivity and 86% specificity, and a score >12 has 100% sensitivity and 94.5% specificity for diagnosing ED (16). The PAED scale differs from the other two scales as it includes elements specific to delirium. The first

three items on the PAED scale score (eye contact, purposeful movement and awareness of surroundings) evaluate the child for disorganised behaviour that is characteristic of delirium. And the last two items (restlessness and inconsolability) are features incorporated into pain scales (16). However, the Watcha scale is easier to use in the recovery room and has the highest sensitivity and specificity (18).

1.5 Outcomes and complications of emergence delirium

A flailing, screaming child results in significant distress and dissatisfaction of the child, parents, recovery staff and surgeons. Such behaviour negatively impacts the recovery room atmosphere and often results in sympathetic agitation in the surrounding children (7). More specifically disorientated children often thrash and bump themselves in their cots resulting in:

- injury to themselves (4, 20, 21) and recovery room staff (4)
- need for additional nursing supervision (21, 22)
- dressing and drain displacement (21)
- injury to surgical site and bleeding (4)
- removal of intravenous cannula that is necessary for administration of drugs to manage ED (4, 21, 22)
- need for supplemental analgesia and sedation that can increase cardio-respiratory complications, postoperative nausea and vomiting (20) and prolong recovery (4, 20, 21).

The odds ratio of new onset postoperative maladaptive behaviour is 1.43 for children with ED in comparison to children without ED (23). It includes general and separation anxiety, regression and withdrawal, sleep and eating disturbances, enuresis and temper tantrums; all of which may persist for up to one year post surgery (24).

1.6 Risk factors for emergence delirium

Although multiple risk factors have been identified, the development of ED remains unpredictable. However, it does allow for preoperative risk stratification, permitting the early implementation of preventative strategies. ED risk factors are categorised into those that are patient, surgery and anaesthetic related.

1.6.1 Patient related risk factors

Young children are thought to be at greater risk of developing ED (3, 14, 23). It may be due to the psychological immaturity of young children to cope with the sudden stress of an unfamiliar environment (14). However, a multi-centre study of 816 patients showed no significant correlation between the age of the child and ED (25). Similar results were produced by another recent study in children having outpatient surgery (15). Additionally, three studies have concluded that gender is not a risk factor of ED (2, 8, 25).

A recent South African study by Swart et al (8) reported an ED odds ratio of 3.67 for Caucasian and Indian (grouped as non-African) children in comparison to African children. The study was conducted at Greys Hospital in Msunduzi, Pietermaritzburg. A notable limitation of the study was the smaller (5%) sample of non-African children in comparison to the much larger (95%) sample of African children. Results of the study included a significant difference in ED incidence between non-African (10.48%) and African children (3.1%) (8). However, because of the disparity in the number of children evaluated in the non-African and African group the result may not be clinically significant.

An inverse relationship was demonstrated between ED and ASA physical status classification in one of the first conducted ED studies. In which, ASA I patients had a higher ED incidence (6.3%) than ASA 4 and 5 patients, who had no incidence of ED (3). Eckenhoff et al (3) suggested that patients required vitality for ED to manifest. And, that the elderly and debilitated patient reacted less to discomfort due to equanimity of advanced age and lethargy. Contradictory to these findings, are those of a robust multi-centre study, that reported no relationship between ED and physical status (25).

Two recent studies reported no significant association between preoperative anxiety and ED (15, 26). However, Kain et al (23) demonstrated that the odds for ED increased by 10% for each increment of 10 points in the modified Yale Preoperative Anxiety Scale (mYPAS). The identifiable risk factors of preoperative anxiety include children with poor social adaptability, shy or inhibited temperament, poor quality of previous medical encounters and maternal anxiety (24). If these risk factors are identified, then the anaesthetist should implement strategies to reduce preoperative anxiety, which may also have the potential to prevent ED.

1.6.2 Surgery related risk factors

Some of the earliest literature noted the correlation between ED and type of surgery. Head and neck procedures seem to provide the highest risk of ED (3, 4, 25). The relative risk of ED following ophthalmic surgery is 1.66 and otologic surgery is 1.69 (4). These procedures are often painful with a short surgical time, resulting in an insufficient time for analgesia to reach peak effect, with children emerging into a painful state that may contribute to ED (4, 15).

Pain can further confound the diagnosis of ED, while being a contributing factor (15). However, ED can also occur in the absence of pain, as demonstrated by an ED incidence of 33% in children who had a sevoflurane general anaesthetic for magnetic resonance imaging (MRI) (13).

1.6.3 Anaesthetic related risk factors

All volatile agents have been associated with ED (4, 27-29). Literature suggests that ED has a stronger association with highly soluble sevoflurane and desflurane, than with the less soluble halothane (27-29). Two meta-analyses demonstrated that ED was more likely to be reported following sevoflurane than propofol anaesthesia (27, 30). A study of recovery profile (emergence time) showed that rapid recovery (following abrupt discontinuation of sevoflurane) and slow recovery (following gradual reduction in sevoflurane), resulted in no significant difference in ED incidence (31). Contrasting results were found by Voepel-Lewis et al (4), who reported that children with ED had a significantly shorter time to awakening from general anesthesia. However, both sevoflurane and propofol result in rapid emergence, yet have vastly different ED incidences (30).

A study reported that the depth of anaesthesia has no relationship to ED (32). However, there was a notable limitation in the study. It utilised bispectral index to evaluate the depth of anaesthesia, which is a tool that bases its algorithm on data from only adult electroencephalograms (EEG), even when used in the paediatric population (32). Lastly, perioperative airway complications have also been identified as a significant risk factor for ED (25).

1.7 Physiology of emergence delirium

This section will discuss noteworthy studies regarding the pathogenesis of ED. However, much further research is required for the pathophysiology to be truly elucidated

1.7.1 Electrical activity of the brain during emergence

Martin et al (33) demonstrated that peaceful emergence was preceded by the following EEG stages – an indeterminate EEG state followed by sleep-like patterns and finally arousal. Children with ED passed directly from an indeterminate EEG state into arousal. The authors described an indeterminate EEG state as an EEG pattern without obvious sleep-like patterns, including slowing of delta frequency and frontally dominant alpha activity, followed by a prolonged state with low voltage and fast frequency EEG activity. Furthermore, after terminating the volatile agent, frontal regional functional connectivity was significantly higher in children with ED in comparison to the controls. The author postulated that increased cortical excitability resulted in elevated frontal connectivity, leading to enhanced sensitivity to stimuli that predisposes a child to ED. However, due to the large variability in paediatric EEG patterns, more robust studies are needed before validated conclusions can be made regarding the general paediatric population (33).

1.7.2 Excitation of the locos coeruleus

Volatile anaesthetics produce a transient period of central nervous system (CNS) excitability followed by depression (34). A small study of volatile and non-volatile anaesthetic effects in the locus coeruleus (LC) of rat brains was conducted (35). The LC has noradrenergic neurons that project to emotional processing and regulating structures such as the cortex, thalamus and hippocampus. Thus, the LC is central to global excitability of the CNS (36, 37). This study demonstrated that sevoflurane directly and significantly increased the rate and magnitude of LC neuron depolarisation. The underlying mechanism is through direct activation of inward currents in the LC neurons, which is thought to be facilitated by hemi-channel and gap junction related effects. Sevoflurane also generated much larger inward currents in the LC neurons than isoflurane and halothane. The LC is

populated with alpha$_{2A}$ adrenoreceptors. An alpha$_{2A}$ adrenoreceptor agonist such as dexmedetomidine resulted in LC neuron hyperpolarisation which prevented the excitatory effects of sevoflurane (35). These findings have yet to be replicated in the human LC.

1.7.3 Changes in brain metabolism

Metabolomics is the study of chemical events that occur at a cellular level by detecting products of metabolism such as glucose. A study (38) of parietal cortex metabolomics of children, during medically indicated MRI using proton magnetic resonance spectroscopy was conducted. The parietal cortex was chosen as it is involved in essential cognitive processes. Additionally, good quality proton magnetic resonance spectroscopy of the parietal lobe has been consistently achieved in comparison to the frontal cortex and hippocampus. The brain MRIs were most commonly indicated for the investigation of headaches, seizure disorders, neurodevelopmental delay and attention deficit hyperactivity disorder. Of these brain MRIs, 43 of the 50 were reported as normal by a neuroradiologist. Children would either receive a sevoflurane or propofol anaesthetic and the PAED scale was used as an evaluation tool in the recovery room (38).

The study demonstrated a significant relationship between the parietal cortex metabolites and the PAED scale score. The total concentration of creatinine negatively correlated to the PAED scale score, whereas lactate and glucose had a positive correlation. For example, if lactate and glucose increased by a total of one millimole, then the PAED scale score increased by approximately 13 points (38).

Sevoflurane and propofol also had different cerebral metabolomic signatures. In the parietal lobe, sevoflurane in comparison to propofol, resulted in a 2-fold greater lactate concentration and a 1.2-fold greater glucose concentration. Children that received sevoflurane had a significantly higher PAED scale score than children that received propofol (38).

1.8 Pharmacological preventative strategies of emergence delirium

This section will briefly discuss some of the pharmacological preventative options.

As stated before volatile agents are associated with ED (4, 27-29) and sevoflurane is more likely to result in ED than propofol (27, 30). Therefore, volatile agents may be avoided, or exposure reduced by an inhalational induction followed by total intravenous anaesthesia. Kocaturk et al (39) reported that the use of propofol in comparison to sevoflurane resulted in a reduction in ED and postoperative pain without increasing emergence and recovery times. A bolus of propofol at the end of surgery also reduced ED incidence and although it lengthened time to awakening, it did not increase recovery time (40, 41).

The use of midazolam remains inconclusive. A meta-analysis by Dahmani et al (42) which included 37 studies concluded that midazolam did not prevent ED, whereas a 2016 meta-analysis reported midazolam to be effective in comparison to a placebo when used as oral premedication or given intravenously intraoperatively (43).

Ketamine has been used successfully via several routes. Ketamine used as an intranasal premedication with oral midazolam significantly reduced ED without delaying emergence and hospital discharge (44). However, the use of ketamine as an oral premedication significantly reduced ED incidence with delayed emergence but without delayed PACU discharge and side effects (45). A meta-analysis by Fang et al (43) also reported that ketamine used intravenously post induction or prior to emergence was more effective in ED prevention than a placebo.

A meta-analysis (46) investigating the use of opioid agonists with sevoflurane anaesthesia reported that premedication with intranasal fentanyl or intraoperative intravenous fentanyl; or intraoperative intravenous remifentanil, sufentanil or alfentanil significantly reduced ED incidence. However, another systematic review (47) concluded that although fentanyl is successful at preventing ED, it should be used at least 10 – 20 minutes before the completion of surgery to prevent prolonged recovery and postoperative nausea and vomiting.

Apan et al (48) reported that a magnesium sulphate infusion 10 minutes before extubation did not reduce ED incidence and prolonged time to eye opening. However, a 2017 meta-analysis concluded that magnesium sulphate used as an intravenous bolus or infusion intraoperatively significantly reduced the incidence of ED (49).

A recent meta-analysis reported that the use of clonidine and dexmedetomidine used via several routes resulted in an overall risk reduction of 0.45 and 0.37 respectively in the development of ED (27).

Although not routinely used, melatonin and gabapentin used as oral premedication have also been successful (50, 51).

A meta-analysis reported that the following drugs significantly reduced ED occurrence in comparison to a placebo. The odds ratios (OR) are as follows: dexmedetomidine OR 0.19, midazolam OR 0.22, propofol OR 0.23, fentanyl OR 0.25, and ketamine OR 0.28. These results suggest that dexmedetomidine should be the first choice, furthermore it is the only one of the listed drugs that does not cause respiratory depression, postoperative nausea and vomiting and prolonged sedation.

1.9 Non-pharmacological preventative strategies of emergence delirium

The South African public health sector is challenged with the burden of an enormous patient load and limited resources (52). The pharmacological management of ED can unfortunately result in prolonged postoperative sedation, cardio-respiratory complications and postoperative nausea and vomiting (20). All of which can lengthen the recovery time and even the hospital stay (20, 21), further increasing hospital costs. The use of non-pharmacological interventions circumvents most of these complications, with the potential to increase theatre productivity. However, the study of non-pharmacological preventative strategies remains in its infancy. The following section highlights some of these novel non-pharmacological interventions.

1.9.1 Non-pharmacological management of preoperative anxiety

Kain et al (53) described the ADVANCE family-centered approach to preoperative anxiety. The ADVANCE acronym is as follows,

Anxiety reduction is the aim of the program

Distraction on the day of surgery with age appropriate toys

Video modelling and education prior to surgery

Adding parents to the surgical experience including induction

No excessive reassurance of the child by parents

Exposure of the child to the induction mask

In this study children were divided into the following four intervention groups: control group, ADVANCE group, midazolam group and a parental presence group. Children in the ADVANCE group and the midazolam group displayed a similar reduction in preoperative anxiety. Additionally, children in the ADVANCE group had a lower incidence of ED, required less analgesia and had a shorter recovery time than all the other children (53).

ONE VOICE (54) is a multidisciplinary strategy with the aim of providing children with a non-threatening hospital environment. The strategy has been successfully applied in hospitals internationally. It resembles the ADVANCE approach, with the addition of an integral component that limits the child to listen and hear only a single voice in theatre. It is thought to reduce the anxiety and stress associated with the hospital experience (54).

Other novel strategies to reduce preoperative anxiety in children include the transport of children to theatre in a toy train (55) and the use of clown doctors and video games (56).

1.9.2 Minimising preoperative fasting

Children often endure lengthy preoperative fasting periods, which often exceed the recommended guidelines due to a lack of medical personnel knowledge, long theatre lists and further delays. The ensuing hunger and thirst of the child can contribute to preoperative anxiety of both the child and parents (57).

A recent study reported that prolonged fasting time may be a risk factor for ED (9). Khanna et al (9) evaluated children following ophthalmic surgery for ED. The results demonstrated that the higher PAED scale scores at 15 and 20 minutes correlated with longer preoperative fasting periods. However, there was no correlation between the fasting blood glucose and the duration of fasting, or with the fasting blood glucose and the PAED scale score at any time. Furthermore, the study did not evaluate preoperative anxiety, therefore the relationship between preoperative anxiety and duration of fasting could not be investigated. Thus, it is uncertain whether it was the increased preoperative anxiety secondary to fasting, or the physiology of prolonged fasting that contributed to the development of ED.

1.9.3 Visual preconditioning prior to ophthalmic surgery

In a study by Lin et al (10) visual preconditioning before ophthalmic surgery was achieved by the application of an eyepatch for more than three hours the day before surgery. There was no significant difference in mYPAS and therefore preoperative anxiety between the visual preconditioning and control groups. Despite this, the visual preconditioning group had a significantly lower ED incidence than the control group, with a reported odds ratio of 4.0 (10).

1.9.4 Use of a laryngeal mask airway instead of an endotracheal tube

The use of a laryngeal mask airway (LMA) has been shown to result in a significantly lower incidence of ED, less postoperative laryngeal pain and shorter recovery times in comparison to the use of a nasal endotracheal tube during dental surgery (58). Furthermore, in this study the use of an LMA did not interfere with dental access or with surgeon satisfaction (58). Endotracheal tubes have also been shown to result in a greater incidence of respiratory complications such as hoarseness and laryngospasm during emergence in comparison to an LMA,

without a significant difference in regurgitation and success of insertion at first attempt (59). Therefore, the use of an LMA may be highly favourable but requires further study.

1.9.5 Acupuncture and electrical stimulation of heart site 7

In South Africa, acupuncture is recognised as an Allied Health modality (60). During acupuncture fine needles, heat or electrical stimulation are applied at specific points in the body which reflect disharmony in order to restore Qi (vital energy), that travels through meridians (channels) in the body (61). Heart site 7 is located at the wrist crease on the radial side of the flexor carpi ulnaris tendon. The stimulation of heart site 7 with acupuncture needles (62) and capsicum plasters (63) reduce ED incidence. A peripheral nerve stimulator, a more practical and common piece of theatre equipment, used at heart site 7 has also been shown to significantly decrease ED incidence (64).

1.9.6 Listening to a recording of the mother's voice

A study by Byun et al (11) demonstrated that children who listened to a recording of their mother's voice displayed a reduced incidence of ED in comparison to children who listened to a recording of a stranger's voice (11). The recording was taken in a calm environment and played repetitively through noise cancelling headphones at the end of surgery. The authors suggested that the results were secondary to the positive emotional responses evoked by the mother's voice, often associated with feeding and soothing and familiar from the last few weeks of gestation. A study titled "Mom called me!" reported that 6-month old infants are more sensitive to their own names and even more so when spoken in their mother's voice in comparison to other names and strangers' voices (65).

1.10 Treatment of emergence delirium

The implementation of preoperative prevention in children identified with ED risk factors is the mainstay of ED management. There is a paucity of literature concerning ED postoperative management. Gentle physical restraint is often employed to prevent injury to the child (22). If the episode persists, the anaesthetist must weigh the potential for child injury versus drug complications (20). If pain is thought to be contributing then an analgesic may be titrated slowly, but if the child has had a non-painful procedure then a sedative drug may be more appropriate (20). A survey completed by the members of the

Canadian Pediatric Anesthesia Society reported that the most often to least used drugs are propofol, midazolam, fentanyl, morphine and dexmedetomidine (66). The use of these drugs can however result in postoperative sedation, cardio-respiratory complications and postoperative nausea and vomiting, all of which may lengthen recovery time (20, 21).

1.11 Conclusion

ED is unfortunately a commonly faced challenge by anaesthetists (4, 8-15). It has the potential of not only acute injury to the child (4, 20, 21), but it may also result in negative postoperative maladaptive behaviours (23, 24). Therefore, the prudent anaesthetist has a depth of ED knowledge, including non-pharmacological strategies, which have the potential for improved patient outcomes and theatre productivity (4, 20, 21). As research continues, we will hopefully gather more insight into ED pathophysiology, which will provide the anaesthetist with a more definitive armamentarium to successfully prevent and treat ED

1.12 References

1. Guedel A. CYCLOPROPANE ANESTHESIA. Anesthesiology. 1940;1(1):13-25. Available: https://anesthesiology.pubs.asahq.org/article.aspx?articleid=1973731 (Accessed 20.8.18)
2. Smessaert A, Schehr CA, Artusio JF. OBSERVATIONS IN THE IMMEDIATE POSTANAESTHESIA PERIOD II. MODE OF RECOVERY. Br J Anaesth. 1960;32(4):181-5. DOI:10.1093/bja/32.4.181
3. Eckenhoff JE, Kneale DH, Dripps RD. THE INCIDENCE AND ETIOLOGY OF POSTANESTHETIC EXCITEMENT. A clinical survey. Anesthesiology. 1961;22(5):667-673. Available: https://anesthesiology.pubs.asahq.org/article.aspx?articleid=1967759 (Accessed 18.8.18)
4. Voepel-Lewis T, Malviya S, Tait AR. A Prospective Cohort Study of Emergence Agitation in the Pediatric Postanesthesia Care Unit. Anesth Analg. 2003;96(6):1625-30. DOI:10.1111/j.1460-9592.2011.03646.x
5. Malarbi S, Stargatt R, Howard K, Davidson A. Characterizing the behavior of children emerging with delirium from general anesthesia. Paediatr Anaesth. 2011;21(9):942-50. DOI: 10.1111/j.1460-9592.2011.03646.x
6. Lerman J. Emergence delirum and agitation in children. Uptodate. 2018. Available: https://www.uptodate.com/contents/emergence-delirium-and-agitation-in-children?search=emergence%20delirium&source=search_result&selectedTitle=1~94&usage_type=default&display_rank=1 (Accessed 18.8.18)
7. Nair S, Wolf A. Emergence delirium after paediatric anaesthesia: new strategies in avoidance and treatment. BJA Educ. 2018;18(1):30-3. DOI: 10.1016/j.bae.2017.07.001
8. Swart ED, Rajah C, Rodseth RN. Induction behaviour and race and its association with postoperative agitation in paediatric elective surgery. SAJAA. 2018;23(2):36-9. DOI: 1080/22201181.2017.1293385
9. Khanna P, Saini K, Sinha R, Nisa N, Kumar S, Maitra S. Correlation between duration of preoperative fasting and emergence delirium in pediatric patients undergoing opthalmic examination under anesthesia: A prospective

observational study. Pediatr Anesth. 2018;28(6):547-51. DOI: 10.1111/pan.13381

10. Lin Y, Shen W, Liu Y, Wang Q, Chen Q, Fang Z, et al. Visual preconditioning reduced emergence delirium in children undergoing opthalmic surgery: a randomised controlled trial. Br J Anaesth. 2018;121(2):476-82. DOI: 10.1016/j.bja.2018.03.033
11. Byun S, Song S, Kim JH, Ryu T, Jeong MY, Kim E. Mother's recorded voice on emergence can decrease postoperative emergence delirium from general anaesthesia in paediatric patients: a prospective randomised controlled trial. Br J Anaesth. 2018;121(2):483-9. DOI: 10.1016/bja.2018.01.042
12. Jooma Z. 2015. Emergence delirium in children undergoing dental surgery under general anaesthesia (M Med). Johannesburg, South Africa The University of the Witwatersrand.
13. Cravero J, Surgenor S, Whalen K. Emergence agitation in paediatric patients after sevoflurane anaesthesia and no surgery: a comparison with halothane. Paediatr Anaesth. 2000;10(4):419-424. DOI: 10.1046/j.1460-9592.2000.00560.x
14. Aono J, Ueda W, Mamiya K, Takimoto E, Manabe M. Greater Incidence of Delirium during Recovery from Sevoflurane Anesthesia in Preschool Boys. Anesthesiology. 1997;87(6):1298-1300. Available: https://anesthesiology.pubs.asahq.org/article.aspx?articleid=1948647 (Accessed 23.8.18)
15. Barreto ACTP, Paschoal ACRR, Farias CB, Borges PSGN, Andrade RGAC, de Orange FA. Risk factors associated with anaesthesia emergence delirium in children undergoing outpatient surgery. Rev Bras Anestesiol. 2018;68(2):162-7. DOI: 10.1016/j.bjane.2017.11.002
16. Sikich N, Lerman J. Developement and Psychometric Evaluation of Pediatric Anesthesia Emergence Delirium Scale. Anesthesiology. 2004;100(5):1138-45. Available: https://anesthesiology.pubs.asahq.org/article.aspx?articleid=1942731 (Accessed 23.8.18)
17. Watcha MF, Ramirez-Ruiz M, White P, Jones MB, Lagueruela RG, Terkonda RP. Perioperative effects of oral ketrolac and acetaminophen in children undergoing bilateral myringotomy. Can J Anaesth. 1992;39(7):649-54.

Available: https://link.springer.com/content/pdf/10.1007/BF03008224.pdf (Accessed 12.4.19)

18. Bajwa SA, Costi D, Cyna AM. A comparison of emergence delirium scales following general anesthesia in children. Pediatr Anesth. 2010;20(8): 704-11. DOI: 10.1111/j.1460-9592.2010.03328.x
19. Ringblom J, Wåhlin I, Prockowska M. A psychometric evaluation of the Pediatric Anaesthesia Emergence Delirium scale. Paediatr Anaesth. 2018;28(4):332-7. DOI: 10.1111/pan.13348.
20. Collins CE, Everett LL. Challenges in Paediatric Ambulatory Anesthesia: Kids are Different. Anesthesiol Clin. 2010;28(2):315-28. DOI: 10.1016/j.anclin.2010.02.005
21. Vlajkovic GP, Sindjelic RP. Emergence Delirium in Children: Many Questions, Few Answers. Anesth Analg. 2007;104(1):84-91. DOI: 10.1213/01.ane.0000250914.91881.a8
22. Banchs RJ, Lerman J. Preoperative Anxiety Management, Emergence Delirium, and Postoperative Behavior. Anesthesiol Clin. 2014;32(1):1-32. DOI: 10.1016/j.anclin.2013.10.011
23. Kain ZN, Caldwell-Andrews AA, Maranets I, McClain B, Gaal D, Mayes LC, et al. Preoperative Anxiety and Emergence Delirium and Postoperative Maladaptive Behaviors. Anesth Analg. 2004;99(6):1648-54. DOI: 10.1213/01.ANE.0000136471.36680.97
24. Kain ZN, Mayes LC, O'Connor TZ, Cicchetti DV. Preoperative Anxiety in children: Predictors and Outcomes. Arch Pediatr Adolesc Med. 1996;150(12):1238-45. DOI: 10.1001/archpedi.1996.02170370016002
25. Chung CJ, Choi S, Park S. Risk factors of emergence agitation after general anesthesia in children; multicenter study. EJA. 2013;30:157-8. Available: https://journals.lww.com/ejanaesthesiology/Fulltext/2013/06001/Risk_factors_of_emergence_agitation_after_general.491.aspx (Accessed 19.9.2018)
26. Joo J, Lee S, Lee Y. Emergence delirium is related to the invasiveness of strabismus surgery in preschool-age children. J Int Med Res. 2014;42(6):1311-22. DOI: 10.1177/0300060514549783
27. Costi D, Cyna AM, Ahmed S, Stephens K, Stickland P, Ellwood J, et al. Effects of sevoflurane versus other general anaesthesia on emergence

agitation in children (Review). Cochrane Database Syst Rev. 2014; Issue 9. Art No: CD007084. DOI: 10.1002/14651858.CD007084.pub2

28. Kuratani N, Oi Y. Greater Incidence of Emergence Agitation in Children after Sevoflurane Anesthesia as Compared with Halothane: a meta-analysis of randomized controlled trials. Anesthesiology. 2008;109(2):225-32. DOI: 10.1097/ALN.0b013e31817f5c18
29. Lim BG, Lee IO, Ahn H, Lee DK, Won YJ, Kim HJ, et al. Comparison of the incidence of emergence agitation and emergence times between desflurane and sevoflurane anesthesia in children. A systematic review and meta-analysis. Med (Baltimore). 2016;95(38):e4927. DOI:10.1097/MD.0000000000004927
30. Kanaya A, Kuratani N, Satoh D, Kurosawa S. Lower incidence of emergence agitation in children after propofol anesthesia compared with sevoflurane: a meta-analysis of randomized controlled trials. J Anesth. 2014;28(1):4-11. DOI: 0.1007/s00540-013-1656-y.
31. Oh AY, Seo KS, Kim CS, Kim HS. Delayed emergence process does not result in lower incidence of emergence agitation after sevoflurane anesthesia in children. Acta Anaesthesiol Scand. 2005;49:297-99. DOI: 10.1111/j.1399-6576.2005.00687.x
32. Frederick HJ, Wofford K, de Lisle Dear G, Schulman S. A Randomized Controlled Trial to Determine the Effect of Depth of Anesthesia on Emergence Agitation in Children. Anesth Analg. 2016;122(4):1141-6. DOI: 10.1213/ANE.0000000000001145
33. Martin JC, Liley DTJ, Harvey AS, Kuhlmann L, Sleigh JW, Davidson AJ. Alterations in the Functional Connectivity of Frontal Lobe Networks Preceding Emergence Delirium in Children. Anesthesiology. 2014;121(4):740-52. DOI: 10.1097/ALN.0000000000000376
34. Milner A, Welch E. Applied Pharmacology in Anaesthesiology and Critical Care. 2nd Ed. Centurion. 2012.
35. Yasui Y, Masaki E, Kato F. Sevoflurane Directly Excites Locus Coeruleus Neurons of Rats. Anesthesiology. 2007;107(6):992-1002. DOI: 10.1097/01.anes.0000291453.78823.f4
36. Aston-Jones G, Chen S, Zhu Y, Oshinsky ML. A neural circuit for circadian regulation of arousal. Nat Neurosci. 2001;4(7):732-8. DOI: 10.1038/89522

37. Aston-Jones G, Chiang C, Alexinsky T. Discharge of noradrenergic locus coeruleus neurons in behaving rats and monkeys suggests a role in vigilance. Prog Brain Res. 1991;88:501-20. DOI: 10.1016/S0079-6123(08)63830-3
38. Jacob Z, Li H, Makaryus R, Zhang S, Reinsel R, Lee H, et al. Metabolomic Profiling of Chidlren's Brains Undergoing General Anesthesia with Sevoflurane and Propofol. Anesthesiology. 2012;117(5):1062-71. DOI: 10.1097/ALN.0b013e31826be417
39. Kocaturk O, Keles S. Recovery characteristics of total intravenous anesthesia with propofol versus sevoflurane anesthesia: a prospective randomized clinical trial. J Pain Res. 2018;11:1289-95. DOI: 10.2147/JPR.S164106.
40. Van Hoff SL, O'Neil ES, Cohen LC, Collins BA. Does a prophylactic dose of propofol reduce emergence agitation in children receiving anesthesia? A systematic review and meta-analysis. Paediatr Anaesth. 2015;25(7):668-76. DOI: 10.1111/pan.12669
41. Aouad MT, Yazbeck-Karam VG, Nasr VG, El-Khatib MF, Kanazi GE, Bleik JH. A Single Dose of Propofol at the End of Surgery for the Prevention of Emergence Agitation in Children Undergoing Strabismus Surgery during Sevoflurane Anesthesia. Anesthesiology. 2007;107(5):733-8. DOI: 10.1097/01.anes.0000287009.46896.a7
42. Dahmani S, Stany L, Brasher C, Lejeune C, Bruneau B, Wood C, et al. Pharmacological prevention of sevoflurane- and desflurane-related emergence agitation in children: a meta-analysis of published studies. Br J Anaesth. 2010;104(2):216-23. DOI: 10.1093/bja/aep376
43. Fang XZ, Gao J, Ge YL, Zhou LJ, Zhang Y. Network Meta-Analysis on the Efficacy of Dexmedetomidine, Midazolam, Ketamine, Propofol, and Fentanyl for the Prevention of Sevoflurane-Related Emergence Agitation in Children. Am J Ther. 2016;23(4):1032-42. DOI: 10.1097/MJT.0000000000000321
44. Bilgen S, Köner O, Karacay S, Sancar NK, Kaspar EC, Sözübir S. Effect of ketamine versus alfentanil following midazolam in preventing emergence agitation in children after sevoflurane anaesthesia: A prospective randomized clinical trial. J Int Med Res. 2014;42(6):1262-71. DOI: 10.1177/0300060514543039
45. Abdelmawgoud A, Mohy A. Effect of oral dextromethorphan versus oral ketamine on sevoflurane related emergence agitation in children undergoing

adenotonsillectomy. Eqypt J Anaesth. 2012;28(4):243-8. DOI: 10.1016/j.egja.2012.05.005

46. Tan Y, Shi Y, Ding H, Kong X, Zhou H, Tian J. μ-Opioid agonists for preventing emergence agitation under sevoflurane anesthesia in children: a meta-analysis of randomized controlled trials. Paediatr Anaesth. 2016;26(2):139-50. DOI: 10.1111/pan.12815.
47. Kim N, Park JN, Lee JS, Choi T, Kim MS. Effects of intravenous fentanyl around the end of surgery on emergence agitation in chidlren: Systematic review and meta-analysis. Paediatr Anaesth. 2017;27(9):885-92. DOI: 10.1111/pan.13181
48. Apan A, Aykac E, Kazkayasi M, Doganci N, Tahran FD. Magnesium sulphate infusion is not effective on discomfort or emergence phenomenon in paediatric adenoidectomy/ tonsillectomy. Int J Pediatr Otorhinolaryngol. 2010;74(12):1367-71. DOI: 10.1016/j.ijporl.2010.09.004
49. Xie M, Li XK, Peng Y. Magnesium sulfate for postoperative complications in children undergoing tonsillectomies: a systematic review and meta-anaylsis. J Evid Based Med. 2017;10(1):16-25. DOI: 10.1111/jebm.12230.
50. Kain ZN, MacLaren JE, Herrmann L, Mayes L, Rosenbaum A, Hata J, et al. Preoperative Melatonin and Its Effects on Induction and Emergence in Children Undergoing Anesthesia and Surgery. Anesthesiology. 2009;111(1):44-9. DOI: 10.1097/ALN.0b013e3181a91870
51. Salman AE, Camkiran A, Oguz S, Dönmez A. Gabapentin premedication for postoperative analgesia and emergence agitation after sevoflurane anesthesia in pediatric patients. Agri. 2013;25(4):163-8. DOI: 10.5505/agri.2013.98852
52. Ataguba JE, McIntyre D. Paying for and receiving benefits from health services in South Africa: is the health system equitable? Health Policy Plan. 2012;27: i35-i45. DOI: 10.1093/heapol/czs005
53. Kain ZN, Caldwell-Andrews AA, Mayes LC, Weinberg ME, Wang SM, MacLaren JE, et al. Family-centered Preparation for Surgery Improves Perioperative Outcomes in Children. Anesthesiology. 2007;106(1):67-74. Available: https://anesthesiology.pubs.asahq.org/article.aspx?articleid=1922803 (Accessed 18.8.18)

54. Wagers D. 2019. One voice. Available: https://onevoice4kids.com/ (Accessed 29.12.19)
55. Liu PP, Sun Y, Wu C, Xu WH, Zhang RD, Zheng JJ, et al. The effectiveness of transport in a toy car for reducing preoperative anxiety in children: a randomised controlled prospective trial. Br J Anaesth. 2018;121(12):438-44. DOI: 10.1016/j.bja.2018.02.067.
56. Manyande A, Cyna AM, Yip P, Chooi C, Middleton P. Non-pharmacological interventions for assisting the induction of anaesthesia in children (Review). Cochrane Database Syst Rev. 2015; Issue 7. Art No:CD006447. DOI: 10.1002/14651858.CD006447.pub3
57. Chon T, Ma A, Mun-Price C. Perioperative Fasting and the Patient Experience. Cureus. 2017;9(5):e1272. DOI: 10.7759/cureus.1272
58. Keles S, Kocaturk O. Postoperative discomfort and emergence delirium in children undergoing dental rehabilitation under general anesthesia: comparison of nasal tracheal intubation and laryngeal mask airway. J Pain Res. 2018;11:103-10. DOI: 10.2147/JPR.S153637
59. Yu SH, Beirne OR. Laryngeal Mask Airways Have a Lower Risk of Airway Complications Compared With Endotracheal Intubation: A Systematic Review. J Oral Maxillofac Surg. 2010;68(10):2359-76. DOI: 10.1016/j.joms.2010.04.017.
60. South Africa. 1982. Allied Health Professions Act 63. Available: https://ahpcsa.co.za/wp-content/uploads/2015/10/Regulations-1982_as-amended_2.pdf (Accessed 14.9.19)
61. Kaptchuk TJ. Acupuncture: Theory, Efficacy, and Practice. Ann Intern Med. 2002;136(5):374-83. DOI: 10.7326/0003-4819-136-5-200203050-00010
62. Lin YC, Tassone RF, Jahng S, Rahbar R, Holzman RS, Zurakowski D, et al. Acupuncture managemnet of pain and emergence agitation in children after bilateral myringotomy and tympanostomy tube insertion. Paediatr Anaesth. 2009;19(110:1096-101. DOI: 10.1111/j.1460-9592.2009.03129.x
63. Acar HV, Yilmaz A, Demir G, Eruyar SG, Dikmen B. Capsicum plasters on acupoints decrease the incidence of emergence agitation in pediatric patients. Paediatr Anaesth. 2012;22(11):1105-9. DOI: 10.1111/j.1460-9592.2012.03876.x

64. Hijikata T, Mihara T, Nakamura N, Miwa T, Ka K, Goto T. Electrical stimulation of the heart 7 acupuncture site for preventing emergence agitation in children: A randomised controlled trial. Eur J Anaesthesiol. 2016;33(7):535-42. DOI: 10.1097/EJA.0000000000000379
65. Imafuku M, Hakuno Y, Uchida-Ota M, Yamamoto JI, Minagawa Y. 'Mom called me!' Behavioural and prefrontal responses of infants to self names spoken by their mothers. Neuroimage. 2014;103:627-33. DOI: 10.1016/j.neuroimage.2014.08.034
66. Rosen HD, Mervitz D, Cravero JP. Pediatric emergence delirium: Canadian Pediatric Anesthesiologists' experience. Paediatr Anesth. 2016;26(2):207-12. DOI: 10.1111/pan.12812

Section 2: Author's guidelines

Southern African Journal of Anaesthesia and Analgesia (SAJAA)

How to submit your paper online:

1. Registered authors must login to submit a paper
    1. REGISTER HERE if you do not have a username and password
    2. LOGIN HERE if you have already registered with SAJAA
2. Select Author
3. Click on CLICK HERE TO FOLLOW THE FIVE STEPS TO SUBMIT YOUR MANUSCRIPT
4. Follow the five steps to submit your paper
5. To view a video on how to submit a paper online CLICK HERE
6. To download instructions to authors CLICK HERE

Review policy and timelines

1. Immediate notification if submitted successfully
2. Notification within 3 weeks if not accepted for further review
3. Notification within 3 months if accepted for publication, if revisions are required or if rejected by both reviewers.
4. Publication within 6 months after submission.

Aims, scope and review policy

The SA Journal of Anaesthesia and Analgesia aims to publish original research and review articles of relevance and interest to the anaesthetist in academia, public sector and private practice. Papers are peer reviewed to ensure that the contents are understandable, valid, important, interesting and enjoyed. All manuscripts must be submitted online.

SAJAA is accredited by the Department of Education for the measurement of research output of public higher institutions of South Africa (SAPSE accredited). All articles in SAJAA will be peer reviewed.

Article sections and length

The following contributions are accepted (word counts exclude abstracts, tables and references):

- Original Research (2 800 – 3 200 words / 4-5 pages)
- Clinical Reviews (2 400 words / 3-4 pages)
- Drug Reviews (2 400 words / 3-4 pages)
- Case Studies (1 800 words / 3 pages)
- Scientific Letters (2 400 words / 3-4 pages)
- Letters to the Editor (400-800 words]

Please see the journal's section policies section policies for further details.

FULL AUTHOR GUIDELINES

Title page

All articles must have a title page with the following information and in this particular order: Title of the article; surname, initials, qualifications and affiliation of each author; The name, postal address, e-mail address and telephonic contact details of the corresponding author and at least 5 keywords.

Abstract

All articles should include an abstract. The structured abstract for an Original Research article should be between 200 and 230 words and should consist of four paragraphs labeled Background, Methods, Results, and Conclusions. It should briefly describe the problem or issue being addressed in the study, how the study was performed, the major results, and what the authors conclude from these results. The abstracts for other types of articles should be no longer than 230 words and need not follow the structured abstract format.

Keywords

All articles should include keywords. Up to five words or short phrases should be used. Use terms from the Medical Subject Headings (MeSH) of Index Medicus

when available and appropriate. Key words are used to index the article and may be published with the abstract.

Acknowledgements

In a separate section, acknowledge any financial support received or possible conflict of interest. This section may also be used to acknowledge substantial contributions to the research or preparation of the manuscript made by persons other than the authors.

References

Cite references in numerical order in the text, in superscript format (Format> Font> Click superscript). Please do not use brackets or do not use the foot note function of MS Word.

In the References section, references must be typed double-spaced and numbered consecutively in the order in which they are cited, not alphabetically.

The style for references should follow the format set forth in the Uniform Requirements for Manuscripts Submitted to Biomedical Journals (http://www.icmje.org) prepared by the International Committee of Medical Journal Editors. Abbreviations for journal titles should follow Index Medicus format. Authors are responsible for the accuracy of all references. Personal communications and unpublished data should not be referenced. If essential, such material should be incorporated in the appropriate place in the text.

List all authors when there are six or fewer; when there are seven or more, list the first three, then “;et al.”; When citing URLs to web documents, place in the reference list, and use the following format: Authors of document (if available). Title of document (if available). URL. (Accessed [date]).

The following are sample references:

1. Jun BC, Song SW, Park CS, Lee DH, Cho KJ, Cho JH. The analysis of maxillary sinus aeration according to aging process: volume assessment by 3-

dimensional reconstruction by high-resolutional CT scanning. Otolaryngol Head Neck Surg. 2005 Mar;132(3):429-34.

2. Polgreen PM, Diekema DJ, Vandeberg J, Wiblin RT, Chen YY, David S, et al. Risk factors for groin wound infection after femoral artery catheterization: a case-control study. Infect Control Hosp Epidemiol [Internet]. 2006 Jan [cited 2007 Jan 5];27(1):34-7. Available from: http://www.journals.uchicago.edu/ICHE/journal/issues/v27n1/2004069/2004069.web. pdf.

More sample references can be found at:

http://www.nlm.nih.gov/bsd/uniform_requirements.html

Tables

Tables should be self-explanatory, clearly organised, and supplemental to the text of the manuscript. Each table should include a clear descriptive title on top and numbered in Roman numerals (I, II, etc) in order of its appearance as called out in text. Tables must me inserted in the correct position in the text. Authors should place explanatory matter in footnotes, not in the heading. Explain in footnotes all non-standard abbreviations.

For footnotes use the following symbols, in sequence:*,†,‡,§,||,**,††,‡‡

Figures

All figures must be inserted in the appropriate position of the electronic document. Symbols, lettering, and numbering (in Arabic numerals e.g. 1, 2, etc. in order of appearance in the text)

should be placed below the figure, clear and large enough to remain legible after the figure has been reduced. Figures must have clear descriptive titles.

Photographs and images

If photographs of patients are used, either the subject should not be identifiable or use of the picture should be authorised by an enclosed written permission from the subject. The position of photographs and images should be clearly indicated in the

text. Electronic images should be saved as either jpeg or gif files. All photographs should be scanned at a high resolution (300dpi, print optimised). Please number the images appropriately.

Permission

Permission should be obtained from the author and publisher for the use of quotes, illustrations, tables, and other materials taken from previously published works, which are not in the public domain. The author is responsible for the payment of any copyright fee(s) if these have not been waived. The letters of permission should accompany the manuscript. The original source(s) should be mentioned in the figure legend or as a footnote to a table.

Review and action

Manuscripts are initially examined by the editorial staff and are usually sent to independent reviewers who are not informed of the identity of the author(s). When publication in its original form is not recommended, the reviewers' comments (without the identity of the reviewer being disclosed) may be passed to the first author and may include suggested revisions. Manuscripts not approved for publication will not be returned.

Ethical considerations

Papers based on original research must adhere to the Declaration of Helsinki on "Ethical Principles for Medical Research Involving Human Subjects"; and must specify from which recognised ethics committee approval for the research was obtained.

Conflict of interest

Authors must declare all financial contributions to their work or other forms of conflict of interest, which may prevent them from executing and publishing unbiased research. [Conflict of interest exists when an author (or the author's institution), has financial or personal relationships with other persons or organizations that inappropriately influence (bias) his or her opinions or actions.] **Modified from: Davidoff F, et al. Sponsorship, Authorship, and Accountability.

(Editorial) JAMA 2001: 286(10) The following declaration may be used if appropriate: “I declare that I have no financial or personal relationship(s) which may have inappropriately influenced me in writing this paper.”

Submissions and correspondence

All submissions must be made online at www.sajaa.co.za and correspondence regarding manuscripts should be addressed to:

The Editor, SAJAA, E-mail: toc@sajaa.co.za

Note: Ensure that the article ID [reference] number is included in the subject of your email correspondence.

Electronic submissions by post or via email

Authors with no e-mail or internet connection can mail their submissions on a CD to: SAJAA, PO Box 14804, Lyttelton Manor, 0140, Gauteng, South Africa.

All manuscripts will be processed online. Submissions by post or by e-mail must be accompanied by a signed copy of the following indemnity and copyright form. CLICK HERE to download and save it to your computer.

Submissions by email should be send as an attachment to

Tips on Preparing your manuscript

1. Please consult the “Uniform requirements for manuscripts submitted to biomedical journals” at www.icmje.org
2. Please consult the guide on Vancouver referencing methods at: http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=citmed.TOC&depth=2
3. The submission must be in UK English, typed in Microsoft Word or RTF with no double spaces after the full stops, double paragraph spacing, font size 10 and font type: Times New Roman.
4. All author details (Full names, Qualifications and affiliation) must be provided.
5. The full contact details of corresponding author (Tel, fax, e-mail, postal address) must be on the manuscript.
6. There must be an abstract and keywords.

7. References must strictly be in Vancouver format. (Reference numbers must be strictly numerical and be typed in superscript, not be in brackets and must be placed AFTER the full stop or comma.)
8. It must be clear where every figure and table should be placed in the text. If possible, tables and figures must be placed in the text where appropriate. If too large or impractical, they may be featured at the end of the manuscript or uploaded as separate supplementary files.
9. All photographs must be at 300dpi and clearly marked according to the figure numbers in the text. (Figure 1, Table II, etc.)
10. All numbers below ten, without percentages or units, must be written in words.
11. Figure numbers: Arabic, table numbers: Roman

Section 3: Draft article

Effect of caregiver's recorded voice on emergence delirium in children undergoing dental surgery

Marisha Bhagowat, MBBCh, DA (SA)

Juan Scribante, PhD

Helen Perrie, MSc

Thomas Kleyenstuber, MBBCh, DA (SA), FCA (SA)

Department of Anaesthesiology, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand

Corresponding Author

Marisha Bhagowat

Department of Anaesthesiology

Charlotte Maxeke Johannesburg Academic Hospital

Jubilee Road

Parktown, Johannesburg

2196

m.bhagowat@gmail.com

011 488 4344

Key words: emergence delirium, recorded voice, caregiver voice, stranger voice, non-pharmacological

Abstract

Background

Emergence delirium (ED) is a distressing and harmful postoperative complication following general anaesthesia. The aim of this study was to compare the incidence of ED in children listening to either a recording of their caregiver's voice or a stranger's voice, during emergence from general anaesthesia for elective dental surgery, at Rahima Moosa Mother and Child Hospital.

Methods

A prospective, randomised and contextual study design was implemented with convenience sampling. This study included children between 2 – 6 years of age who were randomly assigned to caregiver voice group (Group C) or stranger voice group (Group S).

Results

The ED incidence within the total sample was 11 (16.9%). In Group S, 4 (15.4%) children had ED, whereas in Group C, 7 (25%) children had ED (p=0.475). There was no significant difference in Pediatric Anesthesia Emergence Delirium (PAED) scale and the Face, Legs, Activity, Cry and Consolability (FLACC) scores between the two groups. The time from completion of surgery to first purposeful movement and to tracheal extubation was similar in Groups C and S (p=0.595, p=0.992 respectively). ED management and duration in the recovery room were also similar (p=0.300, p=0.326 respectively). There was an overall strong positive correlation between highest FLACC and highest PAED scale scores (r=0.827, p<0 .0001).

Conclusion

The PAED scale scores and the ED incidence were similar in children who listened to either a recording of their caregiver's voice or a stranger's voice.

Introduction

Emergence delirium (ED) is a self-limiting state of altered consciousness, during which children are characteristically disorientated and inconsolable (1-3). A flailing, screaming child can result in injury and cause great dissatisfaction of both families and medical personnel (2, 3). Additionally, these children are 1.43 times more likely to exhibit postoperative maladaptive behaviours that may persist for up to 14 days (4). In a South African study the incidence of ED following dental surgery was 51.6% (5), which lies within the international range of 10 – 80% (6-11), thus ED is not only a concerning complication, but also a commonly faced challenge.

The South African public health sector is burdened with the disparity of an enormous patient load and limited resources (12). The pharmacological intervention of ED can prolong postoperative sedation, result in cardio-respiratory complications and postoperative nausea and vomiting (13), all of which can lengthen recovery time and hospital stay, further compounding hospital costs (3, 13). Non-pharmacological management may circumvent many of these complications, potentially resulting in a decrease of financial burden and an increase in theatre productivity. An abundance of research concerning ED pharmacological prevention exists, however, the study of non-pharmacological management is still in its infancy. A cost-effective non-pharmacological intervention was investigated by Byun et al (9), which reported that children listening to a recording of their mother's voice in comparison to a stranger's voice significantly reduced the incidence of ED.

The aim of this study was to determine the ED incidence in children listening to either a recording of their caregiver's or a stranger's voice, during emergence from general anaesthesia for elective dental surgery, at Rahima Moosa Mother and Child Hospital (RMMCH).

Methods

A prospective, randomised and contextual study design was implemented. Approval of this study was obtained from the Human Research Ethics Committee (Medical) (M181136) of the University of the Witwatersrand and other relevant authorities. The protocol was registered with the South African National Health Research Database (GP201905036). This study was conducted at RMMCH, an academic regional hospital, between August 2019 and January 2020.

Children between 2 – 6 years of age, who were American Society of Anesthesiologists physical status I or II, who were scheduled for elective dental surgery were enrolled into the study. Written informed consent was obtained from the caregiver of the child and assent was obtained from a child who was six years old. The exclusion criteria in the study included:

- children with deafness or hearing impairment
- children with neurodevelopmental delay
- children with contraindications to inhalational anaesthesia
- children that received premedication
- deviation from the standard anaesthetic protocol
- children that had a laryngospasm at the end of surgery treated with propofol
- caregiver mutism
- children not accompanied by a caregiver
- refusal of consent by caregiver
- refusal of assent by child.

In South Africa extended families play a vital role in child support and care. Therefore, in this study the term caregiver included both parents and extended family members who cared directly for the child.

The sample size calculation was based on the only identified pilot study, by Byun et al (9), which determined ED incidence in children listening to a recording of their mother's voice or a stranger's voice. In the pilot study the mean difference of the first PAED scale score between the two groups was 1.6 with a standard deviation of 2.19. Using these values, an alpha value of 0.05 and a test power of 0.8 a

sample size of at least 30 children in each group was calculated. Convenience sampling was used in this study, followed by the random assignment of children to caregiver voice group (Group C) or to stranger voice group (Group S), according to a randomisation sequence that was generated by RANDOM.ORG (14), an online randomisation tool.

In this study the authors and caregivers were blinded, while a research assistant (RA) remained unblinded. On the morning of surgery one author (MB) identified eligible children in the paediatric ward. MB counselled the caregivers and children and then conducted the preoperative consultations. The RA used an iPhone 6 ® to record both the caregiver, speaking home language and herself, speaking English in a quiet space. The following standard sentences were recorded (9):

(Name of child) wake up. Let us go home. (Name of child) wake up. Open your eyes. Take a deep breath.

English was chosen as it is the most commonly spoken language in RMMCH theatres. The quality of the recordings was checked by the RA.

Children were not prescribed premedication and received a standard anaesthetic by the anaesthetists who were assigned to the dental list. The anaesthetists remained blinded in this study and recorded the modified Yale Preoperative Anxiety Scale (mYPAS) score and the intraoperative details. The caregiver was present in theatre until the child fell asleep. In theatre standard ASA monitoring was placed on the child. An inhalational induction was then achieved via facemask with sevoflurane and oxygen. Once the child was asleep an intravenous line was inserted and propofol was titrated to facilitate intubation with a nasal endotracheal tube. Maintenance of anaesthesia was achieved with sevoflurane, oxygen and air. Normocapnia was maintained with controlled or supported ventilation.

Local anaesthetic was infiltrated by the dental surgeon into the surgical field as the primary analgesic, the dose of which was left to the discretion of the dentist. Intravenous paracetamol (15 mg/kg) was administered as an additional analgesic. Intravenous dexamethasone (0.1 mg/kg) was administered as a prophylactic antiemetic.

At the end of surgery the RA placed the noise cancelling, Puro Sound Lab Junior Jams headphones ® on the child (15). The recorded message was set to play repeatedly at normal speech level. Sevoflurane was then terminated by the anaesthetist and the child was only further stimulated by light touch.

Children were extubated awake in theatre and then transferred to the recovery room. Once in the recovery room the RA removed the headphones, by this time the child had been listening to the recording for approximately 10 – 15 minutes.

In the recovery room MB completed the Pediatric Assessment of Emergence Delirium (PAED) scale score (16) and the Faces, Legs, Activity, Crying and Consolability (FLACC) score (17) at 10 minute intervals. If required MB treated children with ED with intravenous fentanyl (1 mcg/kg), or with oral valeron drops (2.5 mg/kg) if the intravenous catheter had been dislodged. Children were only discharged from the recovery room when calm and once the modified Aldrete criteria had been met (18). All the data were collected on a standardised data collection form.

SPSS software (version 22.0) was used for the data analysis. Continuous variables were reported as means and standard deviations, and categorical variables as frequencies and percentages. The data were compared with independent t-tests and Chi^2 tests, and correlated with Pearson product-moment tests. A p-value less than 0.05 was considered statistically significant.

Results

A total of 71 patients were assessed for eligibility, however, 6 children were excluded resulting in a final sample of 65 participants (Figure 1). Children characteristics and the intraoperative parameters were similar in Groups S and C (Table I and II respectively). The intraoperative complications in Group S included 1 (5%) child that had a laryngospasm and 1 (5%) child that had an iatrogenic hyperglycemic event, and in Group C, 1 child (2.9%) had a lost throat pack that was found in theatre waste.

Figure 1 – CONSORT diagram

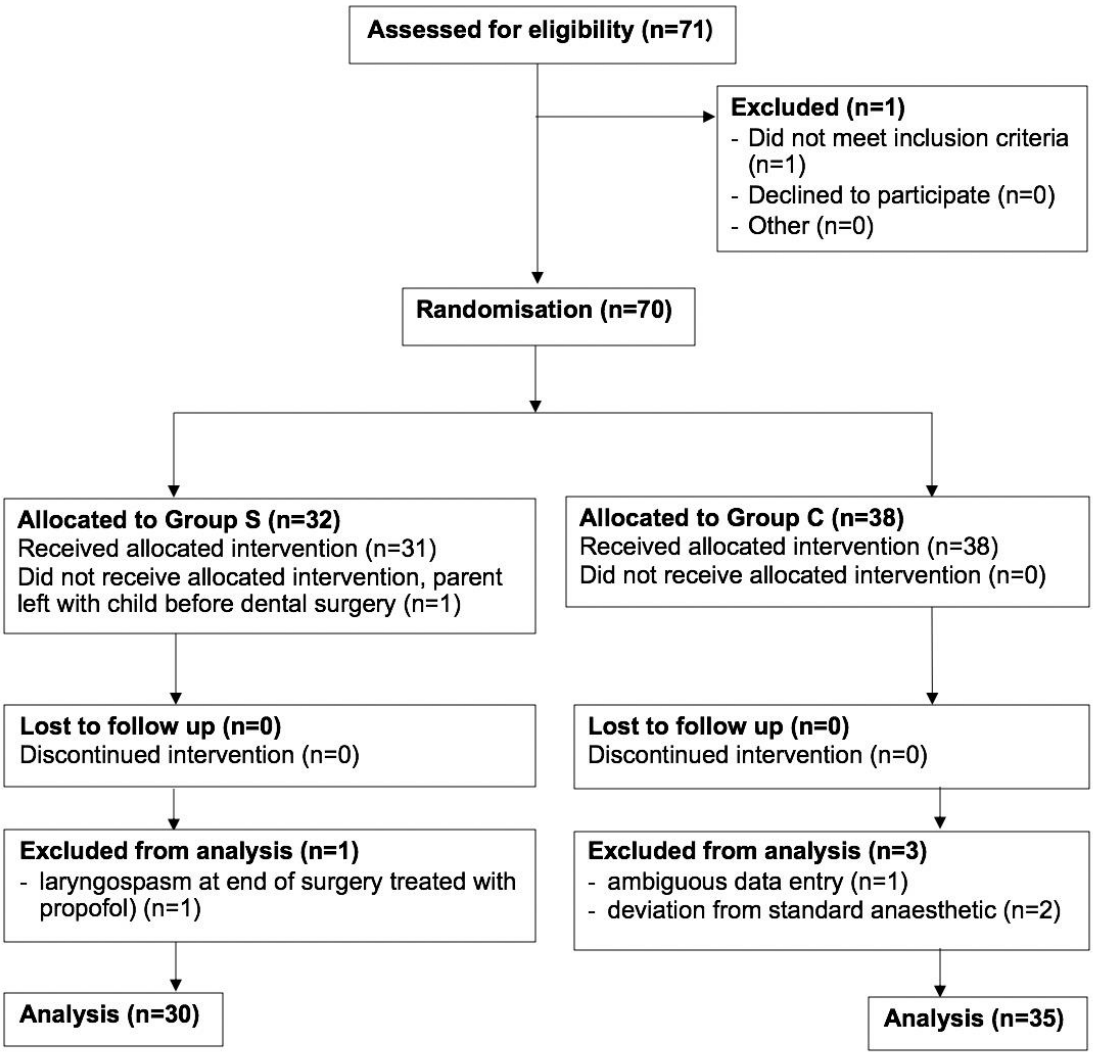


Table I – Children characteristics

	Group S (n=30)	Group C (n=35)	p-value
	mean (SD)	mean (SD)	
Age (months)	53 (10.2)	48.6 (12)	0.119
	n (%)	n (%)	
Sex			
Female	12.0 (40)	18.0 (51.4)	0.357
Male	18.0 (60)	17.0 (48.6)	
ASA			
I	29.0 (96.7)	29.0 (82.9)	0.112
II	1.0 (3.3)	6.0 (17.1)	
Previous anaesthetic			
No	29.0 (96.7)	31.0 (88.6)	0.363
Yes	1.0 (3.3)	4.0 (11.4)	

Table II – Intraoperative and postoperative parameters

	Group S (n=30)	Group C (n=35)	p-value	95% CI for mean difference
Intraoperative parameters	**mean (SD)**	**mean (SD)**		
mYPAS	6.3 (1.7)	6.5 (2.0)	0.644	−1.14 – 0.71
Duration of anaesthesia (minutes)	54.4 (13.2)	49.3 (11.5)	0.100	−1.01 – 11.18
Duration of surgery (minutes)	17.9 (10.0)	17.0 (8.2)	0.672	−3.56 – 5.48
Number of fillings	7.0 (2.3)	6.2 (3.4)	0.274	−0.69 – 2.28
Number of extractions	3.9 (2.7)	4.5 (3.0)	0.412	−2.00 – 0.83
Time from end of surgery to first purposeful movement (minutes)	13.1 (3.6)	12.6 (4.0)	0.595	−1.38 – 2.39
Time from end of surgery to tracheal extubation (minutes)	13.5 (3.7)	13.5 (4.1)	0.992	−1.93 – 1.95
Postoperative parameters				
PAED score in minutes				
0	3.1 (4.9)	3.6 (5.3)	0.659	−3.10 – 1.97
10	1.3 (3.1)	2.0 (3.1)	0.413	−2.18 – 0.91
20	1.3 (2.4)	1.1 (2.2)	0.715	−0.93 – 1.35
30	1.0 (2.1)	0.4 (1.4)	0.217	−0.324 – 1.40
FLACC score in minutes				
0	2.3 (3.3)	2.8 (3.5)	0.585	−2.17 – 1.23
10	1.5 (3.0)	1.8 (2.8)	0.654	−1.76 – 1.13
20	1.5 (3.0)	1.3 (2.1)	0.739	−1.06 – 1.50
30	1.1 (2.3)	0.5 (1.4)	0.185	−0.30 – 1.52
Discharge in minutes				
Ready for discharge	20.1 (7.7)	17.5 (5.1)	0.064	−0.20 – 0.66
Actual discharge	35.2 (1.3)	35.0 (0.0)	0.326	−0.24 – 0.71

There was no significant difference in PAED scale scores between the 2 groups at the observed time intervals (Table II). The ED incidence within the total sample was 11 (16.9%). In Group S, 4 (15.4%) children had ED, whereas in Group C, 7 (25%) children had ED (p=0.475). The mean duration of ED in Group S was 9.3 (3.6) minutes and in Group C it was 6.3 (4.0) minutes (p=0.915).

The FLACC scores and recovery profile at the observed time intervals were similar between the 2 groups (Table II). As shown in table III, the management of ED was similar in Groups S and C (p=0.300). In Group S, 4 (100%) children with ED received intravenous fentanyl, whereas in Group C, 2 (28.6%) children with ED received intravenous fentanyl and 1 (14.3%) child received oral valeron drops. All ED episodes resolved within 5 minutes of drug administration without recurrence The duration of stay in the recovery room was similar between the 2 groups (Table II).

Table III – ED management

	Patients with ED Group S (n=4)	**Patients with ED Group C (n=7)**	**p-value**
	n (%)	**n (%)**	
Restraint only	0.0 (0.0)	1.0 (14.3)	0.300
Restraint plus caregiver	0.0 (0.0)	3.0 (42.9)	
Restraint plus caregiver plus drug	4.0 (100.0)	3.0 (42.9)	

Discussion

In this study the PAED scale scores and the ED incidence were similar in children who listened to a recording of their caregiver's voice or a stranger's voice. Contrasting, are the results of a similar study by Byun et al (9), in which the initial PAED scale scores were significantly reduced in children who listened to a recording of their mother's voice (Group M) in comparison to a stranger's voice (Group S). The initial PAED scale score in Group M was 9.8 (2.5) and in Group S

was 12.5 (4.1). Furthermore, the ED incidence in Group M was 24.2% and in Group S was 60.6% with an odds ratio of 4.88 (p=0.006).

The overall ED incidence in this study was 16.9%. This study was based on the protocol of a previous study at RMMCH, in which the incidence of ED was 51.6% (5). Thus, in comparison to the previous RMMCH study, there is an appreciable reduction in ED. This difference may be due to the use of noise cancelling headphones which limit ambient theatre noise. Noisy theatres of up to 108 dB have been reported, with the greatest noise levels at induction and emergence (19, 20). Therefore, the use of headphones may have reduced noise induced stress, preventing the development of ED. Additionally, the previous study did not evaluate children with the FLACC score, because the use of local anaesthetic is thought to be sufficient following dental surgery on deciduous teeth (21). However, pain may still have been misdiagnosed as ED.

In this study similar results between Groups C and S may have been due to the inadvertent application of non-pharmacological delirium management described in the elderly. Strategies used in the elderly include the use of simple, repetitive language, use of a calm tone, repetitive orientation and noise limitation (22). In this study a recording was played repetitively through noise cancelling headphones, both caregiver and stranger spoke calmly in a quiet environment, with a message that oriented the child to arousal – which may account for the similar results in both groups.

ONE VOICE (23) is a multidisciplinary strategy that has been applied in hospitals internationally, with the aim to provide children with a non-threatening hospital environment. One of the integral components is to only allow the child to listen to one voice while in theatre. Children in Groups C and S were therefore exposed to a described intervention known to reduce both stress and anxiety, which may have played a role in the prevention of ED (23).

Infants have also been shown to be more sensitive to their own names in comparison to a stranger’s name. This was demonstrated in both behaviour (head turning) and functional neuroimaging (24). In this study the name of the child was played repeatedly.

Therefore, the recorded message may have increased arousal and alertness, limiting the disoriented state of ED in both Groups C and S.

Autonomous Sensory Meridian Response (ASMR) is a relatively new concept in which individuals experience relaxation and feelings of well-being accompanied by a tingling skin sensation in response to specific audio and visual stimuli. ASMR has been used in stress and depression management (25). Children in this study may have inadvertently been exposed to ASMR triggers such as personal attention due to repetition of the child's name, and crisp sounds which may have been achieved with the use of noise cancelling headphones with a message spoken by one voice. Therefore, the recordings may have induced a state of relaxation and well-being, combating the development of ED.

Limitations of this study include the use of a sample size calculation that was based on a pilot study set in South Korea, which may have resulted in an inaccurate calculation or an underpowered study. However, the pilot study was used because it was the only study available from which the sample size could be calculated. The PAED scale score was used because it is validated and a commonly used scoring system, however, it is subjective and can result in a loss of consistency during repetitive scoring (16). The dose of local anaesthetic infiltrated by the dental surgeons was not stipulated in the protocol, thus children who may have received insufficient local anaesthetic were at increased risk of ED (7). This study only included South African children undergoing dental surgery, within a specific age range in a single hospital, therefore results may not be generalisable to other populations or to other surgical procedures.

Conclusion

The PAED scale scores and ED incidence are similar in children who listen to either a recording of their caregiver's voice or a stranger's voice. However, in light of a previous study, the use of noise cancelling headphones, or a supportive voice may have the potential to reduce ED incidence, but further investigation is required.

Conflict of interest

The authors declare that we have no financial or personal relationships which may have inappropriately influenced us in writing this paper.

Acknowledgement

This research was done in partial fulfilment of a Master of Medicine degree.

References

1. Malarbi S, Stargatt R, Howard K, Davidson A. Characterizing the behavior of children emerging with delirium from general anesthesia. Paediatr Anaesth. 2011;21(9):942-50. DOI: 10.1111/j.1460-9592.2011.03646.x
2. Nair S, Wolf A. Emergence delirium after paediatric anaesthesia: new strategies in avoidance and treatment. BJA Educ. 2018;18(1):30-3. DOI: 10.1016/j.bae.2017.07.001
3. Vlajkovic GP, Sindjelic RP. Emergence Delirium in Children: Many Questions, Few Answers. Anesth Analg. 2007;104(1):84-91. DOI: 10.1213/01.ane.0000250914.91881.a8
4. Kain ZN, Caldwell-Andrews AA, Maranets I, McClain B, Gaal D, Mayes LC, et al. Preoperative Anxiety and Emergence Delirium and Postoperative Maladaptive Behaviors. Anesth Analg. 2004;99(6):1648-54. DOI: 10.1213/01.ANE.0000136471.36680.97
5. Jooma Z. 2015. Emergence delirium in children undergoing dental surgery under general anaesthesia (M Med). Johannesburg, South Africa The University of the Witwatersrand.
6. Voepel-Lewis T, Malviya S, Tait AR. A Prospective Cohort Study of Emergence Agitation in the Pediatric Postanesthesia Care Unit. Anesth Analg. 2003;96(6):1625-30. DOI:10.1111/j.1460-9592.2011.03646.x
7. Barreto ACTP, Paschoal ACRR, Farias CB, Borges PSGN, Andrade RGAC, de Orange FA. Risk factors associated with anaesthesia emergence delirium in children undergoing outpatient surgery. Rev Bras Anestesiol. 2018;68(2):162-7. DOI: 10.1016/j.bjane.2017.11.002
8. Oh AY, Seo KS, Kim CS, Kim HS. Delayed emergence process does not result in lower incidence of emergence agitation after sevoflurane anesthesia in children. Acta Anaesthesiol Scand. 2005;49:297-99. DOI: 10.1111/j.1399-6576.2005.00687.x
9. Byun S, Song S, Kim JH, Ryu T, Jeong MY, Kim E. Mother's recorded voice on emergence can decrease postoperative emergence delirium from general anaesthesia in paediatric patients: a prospective randomised controlled trial. Br J Anaesth. 2018;121(2):483-9. DOI: 10.1016/bja.2018.01.042

10. Cravero J, Surgenor S, Whalen K. Emergence agitation in paediatric patients after sevoflurane anaesthesia and no surgery: a comparison with halothane. Paediatr Anaesth. 2000;10(4):419-424. DOI: 10.1046/j.1460-9592.2000.00560.x
11. Aono J, Ueda W, Mamiya K, Takimoto E, Manabe M. Greater Incidence of Delirium during Recovery from Sevoflurane Anesthesia in Preschool Boys. Anesthesiology. 1997;87(6):1298-1300. Available: https://anesthesiology.pubs.asahq.org/article.aspx?articleid=1948647 (Accessed 23.8.18)
12. Ataguba JE, McIntyre D. Paying for and receiving benefits from health services in South Africa: is the health system equitable? Health Policy Plan. 2012;27: i35-i45. DOI: 10.1093/heapol/czs005
13. Collins CE, Everett LL. Challenges in Paediatric Ambulatory Anesthesia: Kids are Different. Anesthesiol Clin. 2010;28(2):315-28. DOI: 10.1016/j.anclin.2010.02.005
14. Random.Org. 2018. Available: https://www.random.org/ (Accessed 26.9.18)
15. Puro Sound Labs. 2018. Available: https://purosound.com/products/juniorjams-volume-safe-kids-headphones (Accessed 14.8.18)
16. Merkel SI, Voepel-Lewis T, Shayevitz JR, Malviya S. The FLACC: A Behavioral Scale for Scoring Postoperative Pain in Young Children. Pediatr Nurs. 1997;23(3):293-7. Available: https://www.researchgate.net/publication/13998379_The_FLACC_A_Behavioral_Scale_for_Scoring_Postoperative_Pain_in_Young_Children (Accessed 4.9.18)
17. Sikich N, Lerman J. Developement and Psychometric Evaluation of Pediatric Anesthesia Emergence Delirium Scale. Anesthesiology. 2004;100(5):1138-45. Available: https://anesthesiology.pubs.asahq.org/article.aspx?articleid=1942731 (Accessed 23.8.18)
18. Aldrete JA. The Post-anesthesia Recovery Score Revisited. J Clin Anesth 1995;7(1): 89-91. DOI: 10.1016/0952-8180(94)00001-k
19. Hodge B, Thompson JF. Noise pollution in the operating theatre. Lancet. 1990;335(8694):891-4. DOI: 10.1016/0140-6736(90)90486-O

20. Ginsberg SH, Pantin E, Kraidin J, Solina A, Panjwani S, Yang G. Noise Levels in Modern Operating Rooms During Surgery. J Cardiothorac Vasc Anesth. 2013;27:528-30. DOI: 10.1053/j.jvca.2012.09.001
21. Oosthuizen E. The 'simple' general dental anaesthetic. Contin Med Educ. 2012;30(6):203-6. Avaliable: http://www.cmej.org.za/index.php/cmej/article/view/2444/2355 (Accessed 24.9.18)
22. Grover S, Avasthi A. Clinical Practice Guidelines for Management of Delirium in Elderly. Indian J Psychiatry. 2018;60 (suppl 3):329-40. DOI: 10.4103/0019-5545.224473
23. Wagers D. 2019. One voice. Available: https://onevoice4kids.com/ (Accessed 29.12.19)
24. Imafuku M, Hakuno Y, Uchida-Ota M, Yamamoto JI, Minagawa Y. 'Mom called me!' Behavioural and prefrontal responses of infants to self names spoken by their mothers. Neuroimage. 2014;103:627-33. DOI: 10.1016/j.neuroimage.2014.08.034
25. Barratt EL, Davis NJ. Autonomous Sensory Meridian Response (ASMR): a flow-like mental state. PeerJ. 2005;3:e851. DOI: 10.7717/peerj.851

Section 4: Proposal

Effect of caregiver's recorded voice on emergence delirium in children undergoing dental surgery

Marisha Bhagowat

0603514A

Supervisor: Juan Scribante
Department of Anaesthesiology

Co-supervisor: Helen Perrie
Department of Anaesthesiology

Co-supervisor: Dr Thomas Kleyenstuber
Department of Anaesthesiology

4.1 Introduction and problem statement

Emergence delirium (ED) is an altered state of consciousness, it is the transition from the end of anaesthesia to the return of complete awareness (1). It is self-limiting and usually resolves within 45 minutes (2). Children are characteristically disoriented, inconsolable and unresponsive to even their caregiver (3).

Emergence agitation (EA) is the umbrella term that includes ED and agitation during emergence. Agitation may be due to pathology such as pain, hypotension and hypothermia (4). EA thus encompasses the differential diagnosis of ED, clarifying that the diagnosis of ED is one of exclusion. Emergence excitation is the term often used interchangeably with ED (5).

ED affects 10 to 80% of children (6-10). Notably to this study, are children post dental surgery at Rahima Moosa Mother and Child Hospital (RMMCH), that have an ED incidence of 51.6% (11).

A disoriented, screaming child can result in self-injury and dissatisfaction of both families and medical personnel (2). Additionally these children are 1.43 times more likely to exhibit postoperative maladaptive behaviour that can persist for 14 days (12).

Despite ED having identifiable patient, anaesthetic and surgical-related risk factors it remains unpredictable (2). ED studies (6, 7) conducted in the 1960s reflect many of the following current conclusions. Patient-related risk factors include Non- African children of preschool age and preoperative anxiety (10, 12, 13). Anaesthetic-related risk factors include the use of highly soluble volatiles such as sevoflurane and desflurane (14, 15). Surgical-related risk factors include otorhinolaryngologic and ophthalmic procedures and postoperative pain. Pain is considered both a contributing and confounding factor of ED (13). To overcome this, this study will include children with deciduous teeth, undergoing dental procedures that only require local anaesthetic for analgesia (16).

A variety of ED assessment tools exist, accounting for the discrepancies in diagnosis and epidemiology. In this study the validated and most frequently used Pediatric Anesthesia Emergence Delirium (PAED) scale (Appendix A) will be applied (17).

Little research has been done on the treatment of ED. Some practiced pharmacological interventions include the use of propofol, midazolam, dexmedetomidine and opioids. Once an ED episode has been terminated, whether it be spontaneously or due to treatment, recrudescence has not been reported (4).

A multitude of pharmacological preventative strategies have been researched. Premedication with pregabalin and melatonin, and the use of halothane and propofol for maintenance of anaesthesia have been shown to be effective (18-20). Successful adjuncts include propofol at the end of surgery, dexmedetomidine, clonidine, ketamine, fentanyl, remifentanil and tramadol (20-23).

The South African health sector is challenged with the disparity of an enormous patient load and limited resources. The pharmacological management of ED can prolong postoperative sedation, result in cardio-respiratory complications and postoperative nausea and vomiting. All of which lengthen recovery time and hospital stay, further compounding hospital costs (24). Non-pharmacological management (NPM) circumvents these complications, potentially resulting in a decrease of financial burden and an increase in hospital productivity. A well-studied NPM includes the minimisation of preoperative anxiety through techniques of distraction and parental coaching (25). Novel NPM includes the reduction of preoperative fasting, visual preconditioning prior to ophthalmic surgery, electrical stimulation at acupuncture heart site 7 and use of mother's voice during emergence (8, 9, 26, 27).

Byun et al (27) demonstrated that listening to mother's recorded voice in comparison to a stranger's voice significantly reduced ED incidence. Mother's voice is thought to evoke positive emotional responses because it is a familiar stimulus from late gestation and is associated with feeding and soothing (28). 'Mom called me!' (29) demonstrated that 6-month-old infants are most sensitive to their own names and even more so when spoken in their mother's voice.

In South Africa extended families play a vital role in child rearing. This study will include both mothers and caregivers in order to provide insight in the development of ED within a South African context.

4.2 Aim and objectives

4.2.1 Aim

The aim is to study the incidence of ED between children listening to either a recording of their caregiver's voice or a stranger's voice, during emergence from general anaesthesia for elective dental surgery, at RMMCH.

4.2.2 Objectives

The primary objectives of the study are to compare the following between the 2 groups:

- PAED scale scores
- the incidence of ED.

The secondary objectives of the study are to:

- correlate the modified Yale Preoperative Anxiety Score (mYPAS) with the highest of the PAED scale scores
- compare time from completion of surgery to purposeful movement
- compare time from completion of surgery to tracheal extubation
- correlate the Face, Legs, Activity, Cry and Consolability (FLACC) score with the highest of the PAED scale scores
- describe the interventions used in the management of ED
- compare duration in recovery room.

4.3 Research assumptions

The following definitions will be used in the study.

PAED scale: the Pediatric Anesthesia Emergence Delirium scale (Appendix A) that will be used in the study to evaluate ED (17).

Emergence delirium: a PAED scale score equal to or greater than 10 (17).

mYPAS: the modified Yale Preoperative Anxiety Scale (Appendix B) that will be used in the study to evaluate preoperative anxiety (30).

Preoperative anxiety: a mYPAS greater than 30 (30).

FLACC score: the Face, Legs, Activity, Cry and Consolability score (Appendix C) that will be used in the study to evaluate postoperative pain. It is a score from zero to 10, the higher the score the greater the pain (31).

Child: a person between two to six years of age.

Caregiver: a person that has a relationship and provides care for the child.

Stranger's voice: a voice of a person that is unfamiliar to the child.

Dental surgery: deciduous teeth extractions, fillings and pulpotomies.

Research assistant (RA): a trained and unblinded person that is not part of the medical team. The RA will record the voices for the study and will check the quality of all recordings. He or she will allocate children to the caregiver or stranger group according to the randomisation sequence. He or she will also place the headphones on the child at the end of surgery to ensure that the researcher and anaesthetist remain blinded in the study.

Anaesthetist: a blinded doctor working in the Department of Anaesthesiology that is assigned to the dental theatre.

ASA classification: the physical fitness classification of the American Society of Anesthesiologists (32).

- ASA I is a healthy patient.
- ASA II is a patient with mild systemic disease.
- ASA III is a patient with severe systemic disease.
- ASA IV is a patient with severe systemic disease that is a threat to life.
- ASA V is a patient not expected to live more than 24 hours irrespective of surgical and non-surgical management.
- ASA VI is a brain dead patient for organ donation.
- E denotes emergency surgery.

4.4 Demarcation of study field

The study will be conducted in the theatre complex of RMMCH. RMMCH is a regional hospital affiliated to the University of the Witwatersrand. It has 338 beds and five theatres. One theatre is dedicated to paediatric surgery and includes a weekly dental list. An average of 316 paediatric dental cases are completed annually.

4.5 Ethical considerations

Approval to conduct the study will be obtained from the Human Research Ethics Committee (Medical) and the Graduate Studies Committee of the Faculty of Health Sciences of the University of the Witwatersrand.

Consent to conduct the study will be obtained from the RMMCH committee and the Heads of the Departments of Dentistry and Anaesthesiology at RMMCH (Appendix D).

Eligible participants will be identified, counselled and invited to participate in the study. An information letter (Appendix E) will be provided to the caregiver, who will then be requested to sign consent to participate in the study (Appendix F) and to record their voice (Appendix G). All children will receive a verbal explanation of the study (Appendix H) because some children cannot read. Children that are six

years will then be requested to sign assent to participate in the study (Appendix I) in the presence of the caregiver.

Anonymity will be ensured by allocating a study number to each participant. A study list (Appendix J) with the participant's name, hospital number and study number will be stored separately. Data collection forms (Appendix K) will not contain identifying information.

Confidentiality will be ensured by allowing only the researcher, research assistant and supervisors to have access to raw data. Raw data will be stored securely in a locked cupboard for six years following completion of the study.

All children requiring an intervention for ED or pain postoperatively will be treated by the researcher. Children will only be discharged from the recovery room once awake and calm.

Beneficence, autonomy and justice will be upheld throughout the study. The study will be conducted with adherence to the principles of the Declaration of Helsinki (33) and the South African Guidelines for Good Clinical Practice (34)

4.6 Research methodology

4.6.1 Research design

This is a prospective, randomised, contextual study.

A prospective study measures an outcome at the time it occurs in a specific population (35). In the study ED will be evaluated in children having dental surgery at RMMCH from April to June 2019.

Randomisation is the assignment of participants to study groups based on chance alone. It is a design that ensures all participants have an equal chance of being placed in the control or intervention group. It results in comparable control and intervention groups (35). In the study randomisation will be accomplished with an online tool (36).

A contextual study is conducted in a specific population in a specific location (37). The study has a well-defined population and location.

4.6.2 Study population

The study will include children presenting for elective dental surgery under general anaesthesia at RMMCH.

4.6.3 Study sample

Sample method

Sample method refers to how participants are selected from a population to be in a study. Sampling is intended to predict outcomes that can be extrapolated to a larger population (35, 38).

In this study convenience sampling will be used. Convenience sampling is the non-random use of the most easily accessible individuals in the sample population (35).

Randomisation will be achieved with an online tool (36) that will provide random allocation of study numbers into caregiver voice or stranger voice group.

Sampling size

The sample size was calculated in consultation with a biostatistician. Byun et al (27) conducted a pilot study of ED incidence with mother's voice versus stranger's voice, the mean difference of the first PAED score between the groups was 1.6 with a standard deviation of 2.19. Using these values with an alpha value of 0.05 and a test power of 0.8 a sample size of 30 in each group is calculated.

Inclusion and exclusion criteria

The inclusion criteria for the study are children:

- two to six years old
- ASA I and II
- scheduled for elective dental surgery.

The exclusion criteria in the study are:

- children with deafness or hearing impairment
- children with neurodevelopmental delay
- children with contraindications to inhalational anaesthesia
- children that received premedication
- deviation from the standard anaesthetic protocol
- children that had a laryngospasm at the end of surgery treated with propofol
- caregiver mutism
- children not accompanied by a caregiver
- refusal of consent by caregiver
- refusal of assent by child.

4.6.4 Data collection

Data collection form

A patient list (Appendix J) with the participant's study number, hospital number, name and group will be completed. A data collection form (Appendix K) adapted from a previous study (11) will be completed for each participant. It is divided into the four following sections.

Section 1 – participant personal details:

- study number
- age in months
- sex
- ASA status
- previous anaesthetic experience
- premedication.

Section 2 – mYPAS:

- activity
- vocalisation
- emotional expressivity

- state of apparent arousal
- use of parents.

Section 3 – intraoperative details:

- details of intraoperative drugs
- time at first purposeful movement
- time at tracheal extubation
- anaesthetic complications and management
- duration of anaesthetic
- details of dental procedure
- duration of surgery.

Section 4 – postoperative details:

- PAED scale score and FLACC score in the recovery room at 10-minute intervals for a total of 30 minutes
- duration of ED
- management of ED
- duration of recovery.

Data collection process

The researcher is blinded in the study. On the morning of the surgery the researcher will identify eligible candidates in the paediatric ward. The researcher will then approach the caregiver and child to counsel them about the study. If the caregiver and child verbally agree to participate then an information letter (Appendix E) will be provided and the caregiver will be requested to sign consent to participate in the study (Appendix F) and to record their voice (Appendix G). All children will receive a verbal explanation of the study (Appendix H) because some children cannot read. A child that is six years will be requested to sign assent to participate in the study (Appendix I) in the presence of the caregiver. The caregiver is blinded in the study. The researcher will complete Section 1 (participant personal details) of the data collection form (Appendix K) during preoperative consultation with the caregiver.

The RA is unblinded in the study. The RA will use an iPhone 6 to record both caregiver (speaking home language) and himself or herself (speaking English) in a quiet space. The following standard sentences will be recorded (27):

(Name of child) wake up. Let us go home. (Name of child) wake up. Open your eyes. Take a deep breath.

English was chosen for the RA (stranger) as it is the most commonly spoken language in RMMCH theatres. The RA will then check the quality of all recordings and allocate children to either the caregiver or the stranger group using the randomisation sequence.

The anaesthetist will be blinded in the study and will complete Section 2 (mYPAS) when the child enters theatre and Section 3 (intraoperative details) of the data collection form.

Participants will receive a standard anaesthetic by the anaesthetists assigned to the dental list. The caregiver will be present in theatre until the child is asleep. Once in theatre standard monitoring such as 3-lead electrocardiogram, pulse oximetry and non-invasive blood pressure will be applied. Inhalational induction will be achieved via facemask with sevoflurane and oxygen. Once the child is asleep an intravenous line will be inserted. Propofol will be titrated to facilitate intubation with a nasal endotracheal tube. Anaesthesia will be maintained with sevoflurane, oxygen and air. Ventilation will be controlled or supported to maintain normocapnia.

Local anaesthetic will be infiltrated in the surgical field by the dental surgeon as the primary analgesic. Intravenous paracetamol (15mg/kg) will be administered as an additional analgesic. Intravenous dexamethasone (0.1mg/kg) will be administered as an antiemetic.

At the end of surgery the RA will place the noise cancelling headphones on the child and select the allocated voice on the iPhone 6. Child appropriate, noise cancelling Puro Sound Lab Junior Jams headphones will be used (39). The recorded message will play repeatedly at a normal speech level. Sevoflurane will then be terminated. Participants will only be stimulated by light touch and the voice recording.

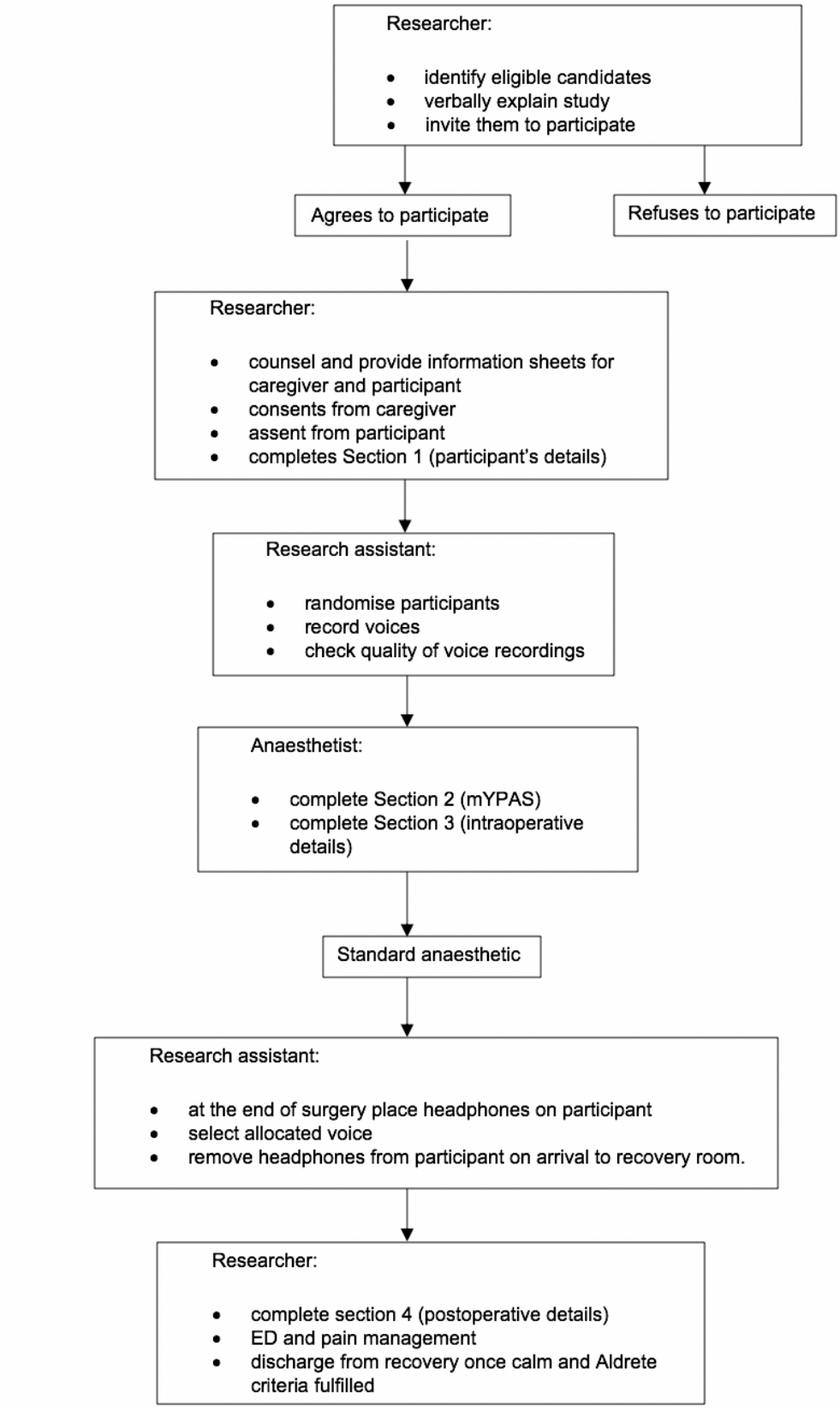
Participants will then be extubated in theatre and transferred to the recovery room. Once in the recovery room the RA will remove the headphones, at this time the child would have been listening to the recording for approximately 10 - 15 minutes. The headphones will be then be cleaned with disinfectant prior to next use.

The researcher will complete Section 4 (postoperative details) of the data collection form. The researcher will treat children requiring an intervention for ED or pain. RMMCH does not have an ED treatment protocol thus treatment will be left to the discretion of the researcher. Children will only be discharged from the recovery room once calm and the Modified Aldrete criteria (40) have been fulfilled.

The blinding will only be broken at the completion of data collection.

The Data collection process is summarised in Figure 1.

Figure 1: Flow diagram summarising the data collection process



4.6.5 Data analysis

Raw data will be transferred onto a spreadsheet on Microsoft Excel. Statistica will be used in consultation with a biostatistician for data analysis. Continuous variables will be reported using means and standard deviations or medians and interquartile ranges depending on the distribution of data. Categorical variables will be reported using frequencies and percentages. The PAED scale scores between the two groups will be compared using independent t-tests. Secondary outcomes such as time from completion of surgery to purposeful movement and tracheal extubation and time to discharge from the recovery room will be compared between the two groups using independent t-tests. The mYPAS and the FLACC scores will be correlated with the highest PAED scale score using either Pearson or Spearman rank correlations. Treatment of ED will be compared using a Chi^2 test. A P value less than 0.05 will be considered statistically significant.

4.7 Significance of the study

A study (11) conducted at RMMCH demonstrated a high incidence of ED. It is therefore imperative that ED management strategies are created within a South African context. This study will potentially provide a NPM to prevent ED and improve parental and child satisfaction. Pharmacological management of ED can prolong postoperative sedation, result in cardio-respiratory complications and postoperative nausea and vomiting (24). All of which lengthen recovery time and hospital stay, further compounding hospital costs. NPM is thus favourable, as it has the potential to decrease financial strain and increase productivity, both of which are desirable in the burdened South African public sector. The study will furthermore provide a strategy tailored to meet the needs of shared child rearing – a prevalent form of care among South African families.

4.8 Validity and reliability of the study

Validity of the study refers to the ability of the study to measure what it was designed to measure (41). Reliability of the study refers to the consistency of results obtained (35, 41).

Validity and reliability of the study will be ensured by the following.

- An appropriate study design will be employed.
- The study population will only include children with deciduous teeth, undergoing dental surgery that only requires local anaesthetic for pain management (16).
- The FLACC score will be performed postoperatively to differentiate and correlate pain with ED.
- The sample size will be determined in consultation with a biostatistician.
- A standard three sentences will be recorded on the same device and quality of the recordings will be checked.
- A standard anaesthetic will be employed to reduce confounding variables.
- Data collection will be completed by a researcher, trained research assistant and anaesthetist to reduce inconsistency.
- The mYPAS will be performed by the same anaesthetist and the PAED and FLACC scores will be performed by the same researcher to prevent inter-observer variation.
- Researcher and anaesthetists will be blinded in the study to reduce observer bias.
- Preoperative anxiety, ED and pain will be measured and diagnosed using validated scales and values.
- Data entries on the Microsoft Excel spreadsheet will be checked.
- Data analysis will be done in consultation with a biostatistician.

4.9 Potential limitations

Study limitations are theoretical or methodological aspects of the study that restrict conclusions of the study results (42).

he study includes South African children of a specific age in a single hospital undergoing dental procedures. Therefore, results of this study are not generalisable to other populations and to other surgical procedures.

4.10 Project outline

4.10.1 Time frame

	Aug 2018	Sept 2018	Oct 2018	Feb 2019	Apr – Jun 2019	Aug 2019	Sept 2019	Oct 2019
Literature review								
Protocol								
Ethics and Postgraduate submission								
Ethics and Postgraduate approval								
Data collection								
Data analysis								
Draft article								
Submission								

4.10.2 Budget

The Department of Anaesthesiology will fund the cost of the paper and photocopying. The Jan Pretorius Foundation will be approached to fund the headphones. The cellphone will be donated. A volunteer will participate as the research assistant. Once the study has been completed the headphones and cellphone will be donated to the department of Anaesthesia for further use.

	Price per item	**Number of items**	**Total**
Paper and photocopying	R1 per page	1500	R1500
Paediatric headphones	R1065	1	R1065
Shipping and delivery cost	R500		R500
Total			R3065

4.11 References

1. Malarbi S, Stargatt R, Howard K, Davidson A. Characterizing the behavior of children emerging with delirium from general anesthesia. Paediatr Anaesth. 2011;21(9):942-50. DOI: 10.1111/j.1460-9592.2011.03646.x
2. Nair S, Wolf A. Emergence delirium after paediatric anaesthesia: new strategies in avoidance and treatment. BJA Educ. 2018;18(1):30-3. DOI: 10.1016/j.bae.2017.07.001
3. Vlajkovic GP, Sindjelic RP. Emergence Delirium in Children: Many Questions, Few Answers. Anesth Analg. 2007;104(1):84-91. DOI: 10.1213/01.ane.0000250914.91881.a8
4. Lerman J. Emergence delirium and agitation in children. Uptodate. 2018. Available: https://www.uptodate.com/contents/emergence-delirium-and-agitation-in children?search=emergence%20delirium&source=search_result&selectedTitle=1~94&usage_type=default&display_rank=1 (Accessed 18.8.18)
5. Banchs RJ, Lerman J. Preoperative Anxiety Management, Emergence Delirium, and Postoperative Behavior. Anesthesiol Clin. 2014;32(1):1-32. DOI: 10.1016/j.anclin.2013.10.011
6. Smessaert A, Schehr CA, Artusio JF. OBSERVATIONS IN THE IMMEDIATE POSTANAESTHESIA PERIOD II. MODE OF RECOVERY. Br J Anaesth. 1960;32(4):181-5. DOI:10.1093/bja/32.4.181
7. Eckenhoff JE, Kneale DH, Dripps RD. THE INCIDENCE AND ETIOLOGY OF POSTANESTHETIC EXCITEMENT. A clinical survey. Anesthesiology. 1961;22(5):667-673. Available: https://anesthesiology.pubs.asahq.org/article.aspx?articleid=1967759 (Accessed 18.8.18)
8. Khanna P, Saini K, Sinha R, Nisa N, Kumar S, Maitra S. Correlation between duration of preoperative fasting and emergence delirium in pediatric patients undergoing opthalmic examination under anesthesia: A prospective observational study. Pediatr Anesth. 2018;28(6):547-51. DOI: 10.1111/pan.13381
9. Lin Y, Shen W, Liu Y, Wang Q, Chen Q, Fang Z, et al. Visual preconditioning reduced emergence delirium in children undergoing opthalmic surgery: a

randomised controlled trial. Br J Anaesth. 2018;121(2):476-82. DOI: 10.1016/j.bja.2018.03.033

10. Swart ED, Rajah C, Rodseth RN. Induction behaviour and race and its association with postoperative agitation in paediatric elective surgery. SAJAA. 2018;23(2):36-9. DOI: 1080/22201181.2017.1293385
11. Jooma Z. 2015. Emergence delirium in children undergoing dental surgery under general anaesthesia (M Med). Johannesburg, South Africa The University of the Witwatersrand.
12. Kain ZN, Caldwell-Andrews AA, Maranets I, McClain B, Gaal D, Mayes LC, et al. Preoperative Anxiety and Emergence Delirium and Postoperative Maladaptive Behaviors. Anesth Analg. 2004;99(6):1648-54. DOI: 10.1213/01.ANE.0000136471.36680.97
13. Voepel-Lewis T, Malviya S, Tait AR. A Prospective Cohort Study of Emergence Agitation in the Pediatric Postanesthesia Care Unit. Anesth Analg. 2003;96(6):1625-30. DOI:10.1111/j.1460-9592.2011.03646.x
14. Lim BG, Lee IO, Ahn H, Lee DK, Won YJ, Kim HJ, et al. Comparison of the incidence of emergence agitation and emergence times between desflurane and sevoflurane anesthesia in children. A systematic review and meta-analysis. Med (Baltimore). 2016;95(38):e4927. DOI:10.1097/MD.0000000000004927
15. Kuratani N, Oi Y. Greater Incidence of Emergence Agitation in Children after Sevoflurane Anesthesia as Compared with Halothane: a meta-analysis of randomized controlled trials. Anesthesiology. 2008;109(2):225-32. DOI: 10.1097/ALN.0b013e31817f5c18
16. Oosthuizen E. The ‘simple’ general dental anaesthetic. Contin Med Educ. 2012;30(6):203-6. Avaliable: http://www.cmej.org.za/index.php/cmej/article/view/2444/2355 (Accessed 24.9.18)
17. Sikich N, Lerman J. Developement and Psychometric Evaluation of Pediatric Anesthesia Emergence Delirium Scale. Anesthesiology. 2004;100(5):1138-45. Available: https://anesthesiology.pubs.asahq.org/article.aspx?articleid=1942731 (Accessed: 23.8.18)

18. Kain ZN, MacLaren JE, Herrmann L, Mayes L, Rosenbaum A, Hata J, et al. Preoperative Melatonin and Its Effects on Induction and Emergence in Children Undergoing Anesthesia and Surgery. Anesthesiology. 2009;111(1):44-9. DOI: 10.1097/ALN.0b013e3181a91870
19. Salman AE, Camkiran A, Oguz S, Dönmez A. Gabapentin premedication for postoperative analgesia and emergence agitation after sevoflurane anesthesia in pediatric patients. Agri. 2013;25(4):163-8. DOI: 10.5505/agri.2013.98852
20. Costi D, Cyna AM, Ahmed S, Stephens K, Stickland P, Ellwood J, et al. Effects of sevoflurane versus other general anaesthesia on emergence agitation in children (Review). Cochrane Database Syst Rev. 2014; Issue 9. Art No: CD007084. DOI: 10.1002/14651858.CD007084.pub2
21. Fang XZ, Gao J, Ge YL, Zhou LJ, Zhang Y. Network Meta-Analysis on the Efficacy of Dexmedetomidine, Midazolam, Ketamine, Propofol, and Fentanyl for the Prevention of Sevoflurane-Related Emergence Agitation in Children. Am J Ther. 2016;23(4):1032-42. DOI: 10.1097/MJT.0000000000000321
22. Choi YH, Kim KM, Lee SK, Kim YS, Kim SJ, Hwang WS, et al. Effects of remifentanil and remifentanil-alfentanil administration on emergence agitation after brief ophthalmic surgery in children. BMC Anesthesiol. 2016;16:50. doi: 10.1186/s12871-016-0213-2
23. Bediril N, Akcabay M, Emik U. Tramadol vs dexmedetomidine for emergence agitation control in pediatric patients undergoing adenotonsillectomy with sevoflurane anesthesia: prospective randomized controlled clinical study. BMC Anesthesiol. 2017;17:41. DOI: 10.1186/s12871-017-0332-4
24. Collins CE, Everett LL. Challenges in Paediatric Ambulatory Anesthesia: Kids are Different. Anesthesiol Clin. 2010;28(2):315-28. DOI: 10.1016/j.anclin.2010.02.005
25. Kain ZN, Caldwell-Andrews AA, Mayes LC, Weinberg ME, Wang SM, MacLaren JE, et al. Family-centered Preparation for Surgery Improves Perioperative Outcomes in Children. Anesthesiology. 2007;106(1):67-74. Available: https://anesthesiology.pubs.asahq.org/article.aspx?articleid=1922803 (Accessed 18.8.18)
26. Hijikata T, Mihara T, Nakamura N, Miwa T, Ka K, Goto T. Electrical stimulation of the heart 7 acupuncture site for preventing emergence agitation in children.

A randomised controlled trial. Eur J Anaesthesiol. 2016;33(7):535-42. DOI: 10.1097/EJA.0000000000000379

27. Byun S, Song S, Kim JH, Ryu T, Jeong MY, Kim E. Mother's recorded voice on emergence can decrease postoperative emergence delirium from general anaesthesia in paediatric patients: a prospective randomised controlled trial. Br J Anaesth. 2018;121(2):483-9. DOI: 10.1016/bja.2018.01.042
28. Purhonen M, Kilpeläinen-Lees R, Valkonen-Korhonen M, Karhu J, Lehtonen J. Four-month-old infants process own mother's voice faster than unfamiliar voices – Electrical signs of sensitization in infant brain. Cogn Brain Res. 2005;24(3):627-33. DOI: 10.1016/j.cogbrainres.2005.03.012
29. Imafuku M, Hakuno Y, Uchida-Ota M, Yamamoto JI, Minagawa Y. "Mom called me!" Behavioural and prefrontal responses of infants to self-names spoken by their mothers. Neuroimage. 2014;103:627-33. DOI: 10.1016/j.neuroimage.2014.08.034
30. Kain ZN, Mayes LC, Cicchetti DV, Bagnall AL, Finley JD, Hofstadter MB. The Yale Preoperative Anxiety Scale: How Does It Compare with a "Gold Standard"? Anesth Analg. 1997;85(4):783-8. Available: http://0-ovidsp.tx.ovid.com.innopac.wits.ac.za/sp-3.31.1a/ovidweb.cgi (Accessed 13.8.18)
31. Merkel SI, Voepel-Lewis T, Shayevitz JR, Malviya S. The FLACC: A Behavioral Scale for Scoring Postoperative Pain in Young Children. Pediatr Nurs. 1997;23(3):293-7. Available: https://www.researchgate.net/publication/13998379_The_FLACC_A_Behavioral_Scale_for_Scoring_Postoperative_Pain_in_Young_Children (Accessed 4.9.18)
32. American Society Of Anesthesiologists. 2014. American Society of Anesthesiologists Physical Status Classification System. Available: https://www.asahq.org/standards-and-guidelines/asa-physical-status-classification-system (Accessed 24.9.18)
33. World Medical Association. 2013. Declaration of Helsinki. Available: https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/ (Accessed 24.9.18)

34. Department Of Health. 2006. Guidelines for Good Practice In the Conduct of Clinical Trials with Human Participants in South Africa. Available: http://www.kznhealth.gov.za/research/guideline2.pdf (Accessed 24.9.18)
35. Brink H, Van Der Walt C, Van Rensburg C. Fundamentals of Research Methodology for Healthcare Professionals. 3rd ed. Cape Town. Juta. 2012.
36. Random.Org. 2018. Available: https://www.random.org/ (Accessed 26.9.18)
37. De Vos A, Strydom H, Fouche C, Poggenpoel M, Schurink E, Schurinck W. Research at Grass Roots: A primer for the caring professions. 2nd ed. Pretoria. Van Schaik. 2000.
38. Endocott R. Clinical research 3: Sample selection. Accid Emerg Nurs. 2007;15(4):234-8. DOI: 10.1016/j.aaen.2006.12.006
39. Puro Sound Labs. 2018. Available: https://purosound.com/products/juniorjams-volume-safe-kids-headphones (Accessed 14.8.18)
40. Aldrete JA. The Post-anesthesia Recovery Score Revisited. J Clin Anesth 1995;7(1): 89-91. DOI: 10.1016/0952-8180(94)00001-k
41. Botma Y, Greef M, Mulaudizi F, Wright S. Research in Health Sciences.1st ed. Cape Town. Heinemann. 2010.
42. Burns N, Grove S. The Practice of Nursing Research: Appraisal, Synthesis and Generation of Evidence. 6th ed. Missouri. Saunders Elselvier. 2009.

4.12 Appendices

Appendix A: Pediatric Anesthesia Emergence Delirium scale

	Description	Not at all	A little	Quite a bit	Very much	Extremely
1	The child makes contact with the caregiver	4	3	2	1	0
2	The child's actions are purposeful	4	3	2	1	0
3	The child is aware of his or her surroundings	4	3	2	1	0
4	The child is restless	0	1	2	3	4
5	The child is inconsolable	0	1	2	3	4

Appendix B: modified Yale Preoperative Anxiety Scale

	Activity
1	Looking around, curious, playing with toys, reading (or other age-appropriate behavior); moves around holding area/ treatment room to get toys or to go to parent; may move toward operating room equipment
2	Not exploring or playing, may look down, fidget with hands, or suck thumb (blanket); may sit close to parent while waiting, or play has a manic quality
3	Moving from toy to parent in unfocused manner, non-activity derived movements; frenetic/ frenzied movement or play; squirming, moving on table; may push mask away or cling to parent
4	Actively trying to get away, pushes with feet and arms, may move whole body; in waiting room, running around unfocused, not looking at toys, will not be separate from parent, desperate clinging
	Vocalization
1	Reads (non-vocalizing appropriate to activity), asking questions, making comments, babbling, laughing, readily answers questions but may be generally quiet; child too young to talk in social situations or too engrossed in play to respond
2	Responding to adults but whispers, ‘baby talk’, only head nodding
3	Quiet, no sounds or responses to adults
4	Whimpering, moaning, groaning, silently crying
5	Crying or may be screaming ‘no’
6	Crying, screaming loudly, sustained (audible through mask)
	Emotional expressivity
1	Manifestly happy, smiling, or concentrating on play
2	Neutral, no visible expression on face
3	Worried (sad) to frightening, sad, worried, or tearful eyes
4	Distressed, crying, extreme upset, may have wide eyes
	State of apparent arousal
1	Alert, looks around occasionally, notices or watches anesthesiologist (could be relaxed)
2	Withdrawn, sitting still and quiet, may be sucking on thumb or face turned to adult
3	Vigilant, looking quickly all around, may startle to sounds, eyes wide, body tense
4	Panicked whimpering, may be crying or pushing others away, turns away
	Use of parents
1	Busy playing, sitting idle, or engaged in age appropriate behaviour and doesn’t need parent; may interact with parent if parent initiates the interaction
2	Reaches out to parent (approaches and speaks to otherwise silent parent), seeks and accepts comfort, may lean against parent
3	Looks to parents quietly, apparently watches actions, doesn’t seek contact or comfort, and accepts it if offered or clings to parent
4	Keeps parent at distance or may actively withdraw from parent, may push parent away or desperately clinging to parent and will not let go

Appendix C: Face, Legs, Activity, Cry and Consolability score

Categories	Scoring		
	0	1	2
Face	No particular expression or smile	Occasional grimace or frown, withdrawn, disinterested	Frequent to constant quivering chin, clenched jaw
Legs	Normal position or relaxed	Uneasy, restless, tense	Kicking, or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid or jerking
Cry	No cry (awake or asleep)	Moans or whimpers, occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching, hugging or being talked to, distractable	Difficult to console or comfort

Appendix D: Letter to RMMCH committee and Head of Department

Dr Marisha Bhagowat

Department of Anaesthesiology

University of the Witwatersrand

m.bhagowat@gmail.com

9 September 2018

Dear RMMCH committee or Head of Department

I am a registrar in the Department of Anaesthesiology. I am conducting a study as part of my Master of Medicine in Anaesthesiology titled: Effect of caregiver's recorded voice on emergence delirium in children undergoing dental surgery.

The study will include children between two to six years presenting for elective dental surgery in theatre. I will be comparing the incidence of emergence delirium in children that listen to a recording of their primary caregiver's voice versus a stranger's voice during emergence. All patients will receive routine care and will not be at risk of harm. Emergence delirium will be treated as per standard practice in the recovery room.

This study has received Ethics and Graduate Studies Committee approval.

This study will not result in additional cost to the hospital.

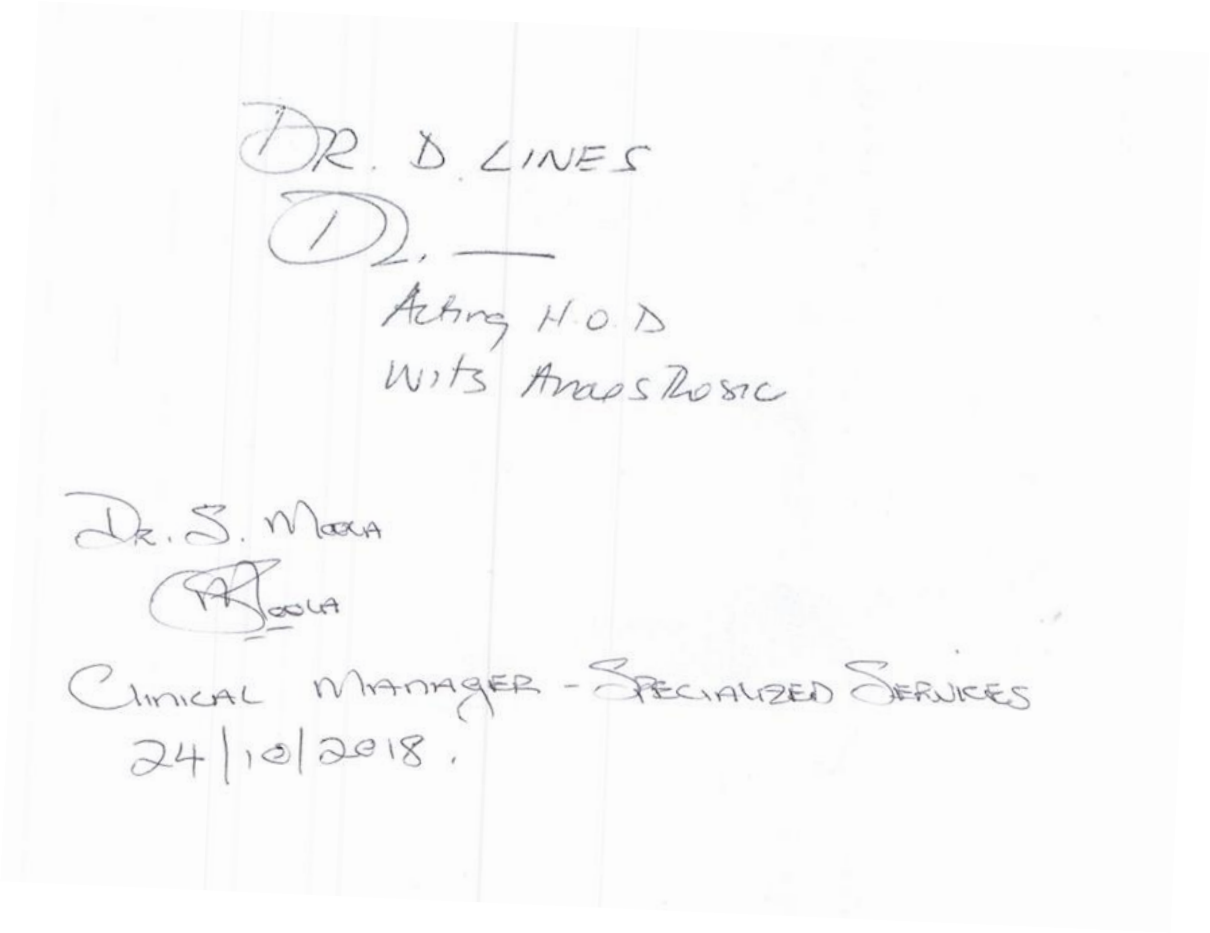
I hereby request permission to conduct research at Rahima Moosa Mother and Child Hospital between April to June 2019. The length of time may be extended if the minimum number of participants have not been recruited during the initial three months.

I have attached the proposal. Please do not hesitate to contact me for further information.

Thanking you in advance.

Kind regards,

Dr Marisha Bhagowat



Appendix E: Information letter

Information for research: Effect of caregiver's recorded voice on emergence delirium in children undergoing dental surgery

Hello. My name is Marisha Bhagowat. I am studying at the University of the Witwatersrand in Johannesburg to become an anaesthesiologist. An anaesthesiologist is a doctor that puts the patient to sleep for an operation and ensures that the patient is pain free and comfortable.

Part of my studies requires that I do a research project. The title of my project is: Effect of caregiver's recorded voice on emergence delirium in children undergoing dental surgery. Emergence delirium occurs when a child wakes up after an operation and is confused, screaming and crying.

I would like to invite you and your child to participate in my research project. The study will investigate if listening to their caregiver's recorded voice while waking up after an operation will reduce emergence delirium.

The purpose of my study is to provide information to develop a non-pharmacological method to help children wake up peacefully after an operation.

Children that participate will be randomly allocated to listen to a recording of their caregiver's or a stranger's voice while waking up after the operation. All children that participate in the study will receive routine care and will not be at risk of harm. Your child may benefit from participating as he or she may wake up more peacefully after the operation. No monetary compensation will be provided for participation in the study.

It is entirely your decision to be in the study. You can also withdraw participation at any time. Even if you do not want to participate in the study your child will receive routine care and will not be at risk of harm. The doctors and nurses will not be upset with you.

A study number will be allocated to your child and the data collection form will only contain the study number and no other identifying information. All data will be stored securely in a locked cupboard for two years post publication and for six years if the research is not published.

If you and your child agree to participate then I will ask you to sign consent forms for participation and to record your voice, if your child is six years then I will ask him or her to sign an assent form. I will also ask you a few questions about your child. A research assistant will then take a short recording of you speaking in your home language saying the following sentences:

(Name of child) wake up. Let us go home. (Name of child) wake up. Open your eyes. Take a deep breath.

All of the above should only take about 10 minutes of your time.

At the end of the operation a research assistant will place noise cancelling headphones on your child and select the randomly allocated voice. After the operation when your child is fully awake I will destroy the recording of your voice.

You will be in theatre with your child while he or she falls sleep. You will then wait outside theatre during the operation. After the operation you will meet your child in the recovery room. I will assess your child every 10 minutes for emergence delirium and pain until 30 minutes after the operation. If your child has emergence delirium I will treat him or her with medication. I will only discharge your child to the ward when he or she is calm and pain free.

If you have any questions, please ask the doctors and nurses. You may contact me on 011 488 4344 and the Chairman of the Ethics Committee (Professor C Penny) on 0117172301.

The study has been approved by the Human Research Ethics Committee (medical) and the Graduate Studies Committee of the University of the Witwatersrand. You may contact the Human Research Ethics Committee (medical) on 011 717 1234.

By signing your name on the consent form, it means that you agree that your child will participate in the study. You will be given a copy of this form to keep.

Thank you for time.

Kind regards,

Dr Marisha Bhagowat

Appendix F: Consent to participate

Consent to participate in research study: Effect of caregiver's recorded voice on emergence delirium in children undergoing dental surgery

I _____ the caregiver (parent or guardian) of the child _____ have been counselled and understand the study. I consent for the above-named child to participate in the study. I have read and understand the information sheet. All my questions have been answered. I understand that my identity and the identity of the child will be protected and concealed at all times. I understand that participation in the study will not harm the child. I know that I may withdraw the child from the study at any time without prejudice toward myself or the child.

_____	_____
Name of primary caregiver	Signature of primary caregiver
_____	_____
Name of researcher	Signature of researcher

Date: _____

Appendix G: Consent to record caregiver's voice

Consent to record caregiver's voice for research study: Effect of caregiver's recorded voice on emergence delirium in children undergoing dental surgery

I _____ the caregiver of the child _____ have been counselled and understand the study. I consent for my voice to be recorded for the study. I know that the recording will be destroyed after the operation when my child is awake. I have read and understand the information sheet. All my questions have been answered. I understand that my identity will be protected and concealed at all times. I know that I may withdraw from the study at any time without prejudice toward myself or the child.

_____ _____

Name of caregiver Signature of caregiver

_____ _____

Name of researcher Signature of researcher

Date: _____

Appendix H: Participant information sheet to be verbally explained to the participating child

Hello. My name is Marisha. I am studying to become a doctor that puts a patient to sleep for an operation.

I must do a research project as part of my studies. I would like to invite you to take part in my study. The study will investigate if listening to a caregiver's recorded voice while waking up after an operation will reduce confusion.

Children that take part will be randomly allocated to listen to a recording of their caregiver's or a stranger's voice while waking up after the operation. All children that take part in the study will receive routine care and will not be at risk of harm.

You may benefit from participating because you may wake up more peacefully after the operation.

It is entirely your decision to be in the study. You can withdraw participation at any time. Even if you do not want to participate in the study you will receive routine care and will not be at risk of harm. The doctors and nurses will not be upset with you.

Your identity will be concealed at all times during data collection.

If you agree to participate and you are six years, then I will ask you to sign an assent form for participation.

Your caregiver will be in theatre with you while you fall asleep for the operation. At the end of the operation a research assistant will place headphones on you. You will wake up listening to either a recording of your caregiver's or a stranger's voice through the headphones. Once you arrive in the recovery area the research assistant will remove the headphones.

I will assess you every 10 minutes for confusion and pain until 30 minutes after the operation. If you are confused I will treat you with medication. I will only send you to the ward once you are calm and pain free.

If you have any questions, please ask me or another doctor or the nurses.

Thank you for your time.

Appendix I: Assent to participate

Assent to participate in research study: Effect of caregiver's recorded voice on emergence delirium in children undergoing dental surgery

Please write your name.

I _____ am happy to participate in the study. I understand what the study is about. All my questions have been answered. I know that I can be taken out of the study at any time and no one will be upset with me. I understand that no one will know that I was part of the study.

_____	_____
Name of child	Signature of child
_____	_____
Name of researcher	Signature of researcher

Date: _____

Appendix J: Study list (page 1)

Patient list for the study: Effect of caregiver's recorded voice on emergence delirium in children undergoing dental surgery

Study no.	Hospital no.	Name	Group
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			
11			
12			
13			
14			
15			

Appendix K: Data collection form

Section 1: Personal details

Date		
Study number		
Age in months		
Sex	Female	Male
ASA status	I	II
Previous anaesthetic	Yes	No
Premedication	Yes	No

Appendix K: Data collection form

Section 2: modified Yale Preoperative Anxiety Score

	Activity
1	Looking around, curious, playing with toys, reading (or other age-appropriate behavior); moves around holding area/ treatment room to get toys or to go to parent; may move toward operating room equipment
2	Not exploring or playing, may look down, fidget with hands, or suck thumb (blanket); may sit close to parent while waiting, or play has a manic quality
3	Moving from toy to parent in unfocused manner, non-activity derived movements; frenetic/ frenzied movement or play; squirming, moving on table; may push mask away or cling to parent
4	Actively trying to get away, pushes with feet and arms, may move whole body; in waiting room, running around unfocused, not looking at toys, will not be separate from parent, desperate clinging
	Vocalization
1	Reads (non-vocalizing appropriate to activity), asking questions, making comments, babbling, laughing, readily answers questions but may be generally quiet; child too young to talk in social situations or too engrossed in play to respond
2	Responding to adults but whispers, ‘baby talk’, only head nodding
3	Quiet, no sounds or responses to adults
4	Whimpering, moaning, groaning, silently crying
5	Crying or may be screaming ‘no’
6	Crying, screaming loudly, sustained (audible through mask)
	Emotional expressivity
1	Manifestly happy, smiling, or concentrating on play
2	Neutral, no visible expression on face
3	Worried (sad) to frightening, sad, worried, or tearful eyes
4	Distressed, crying, extreme upset, may have wide eyes
	State of apparent arousal
1	Alert, looks around occasionally, notices or watches anesthesiologist (could be relaxed)
2	Withdrawn, sitting still and quiet, may be sucking on thumb or face turned to adult
3	Vigilant, looking quickly all around, may startle to sounds, eyes wide, body tense
4	Panicked whimpering, may be crying or pushing others away, turns away
	Use of parents
1	Busy playing, sitting idle, or engaged in age appropriate behaviour and doesn’t need parent; may interact with parent if parent initiates the interaction
2	Reaches out to parent (approaches and speaks to otherwise silent parent), seeks and accepts comfort, may lean against parent
3	Looks to parents quietly, apparently watches actions, doesn’t seek contact or comfort, and accepts it if offered or clings to parent
4	Keeps parent at distance or may actively withdraw from parent, may push parent away or desperately clinging to parent and will not let go
Total	

Appendix K: Data collection form

Section 3: Intraoperative details

Anaesthesia				
Start time				
End time				
Duration (minutes)				
Paracetamol	No	Yes	Dose	
Dexamethasone	No	Yes	Dose	
Other drugs	No	Yes	Drug name	Dose
Time volatile stopped (headphones on)				
Time at first purposeful movement				
Time at extubation				
Anaesthesia complications and management				
Complication	**Management**			
Laryngospasm	No	Yes	Details:	
Bronchospasm	No	Yes	Details:	
Other	No	Yes	Details:	

Surgery	
Start time	
End time	
Duration (minutes)	
No. of teeth worked on	
Dental procedure	

Appendix K: Data collection form

Section 4: Postoperative details

<table>
<tr><td>Time at arrival to recovery room (headphones off)</td><td colspan="4"></td></tr>
<tr><td colspan="5"></td></tr>
<tr><td>Time</td><td colspan="2">PAED score</td><td colspan="2">FLACC score</td></tr>
<tr><td>0 minutes</td><td colspan="2"></td><td colspan="2"></td></tr>
<tr><td>10 minutes</td><td colspan="2"></td><td colspan="2"></td></tr>
<tr><td>20 minutes</td><td colspan="2"></td><td colspan="2"></td></tr>
<tr><td>30 minutes</td><td colspan="2"></td><td colspan="2"></td></tr>
<tr><td colspan="5"></td></tr>
<tr><td colspan="5">If emergence delirium present:</td></tr>
<tr><td>Start time</td><td colspan="4"></td></tr>
<tr><td>End time</td><td colspan="4"></td></tr>
<tr><td>Duration in minutes</td><td colspan="4"></td></tr>
<tr><td rowspan="2">Treatment</td><td rowspan="2">No</td><td rowspan="2">Yes</td><td>Restraint</td><td>Drug:</td></tr>
<tr><td rowspan="2">Caregiver</td><td rowspan="2">Dose:</td></tr>
<tr><td colspan="5"></td></tr>
</table>

Time at discharge to ward	
Duration in recovery room (minutes)	

Section 5: Annexures

5.1 Ethics approval

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Drs M Bhagowat & T Kleyenstuber; Ms H Perrie

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M181138

NAME: **(Principal Investigator)**	Drs M Bhagowat & T Kleyenstuber; Ms H Perrie
DEPARTMENT:	School of Clinical Medicine Department of Anaesthesiology Rahima Moosa Mother and Child Hospital
PROJECT TITLE:	Effect of caregiver's recorded voice on emergence delirium in children undergoing dental surgery
DATE CONSIDERED:	30/11/2018
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Professor J Scribante
APPROVED BY:	CB Penny Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	29/05/2019

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the 3rd Floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.
I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to submit details to the Committee. I agree to submit a yearly progress report. When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **November** and will therefore reports and re-certification will be due early in the month of **November** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature _____ Date _____

PLEASE QUOTE THE CLEARANCE CERTIFICATE NUMBER IN ALL ENQUIRIES

5.2 Graduate studies approval

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Private Bag 3 Wits, 2050
Fax: 027117172119
Tel: 02711 7172076

Reference: Mrs Sandra Benn
E-mail: sandra.benn@wits.ac.za

04 January 2019
Person No: 0603514A
PAG

Dr M Bhagowat
94 Ridgeton Towers
4319
South Africa

Dear Dr Marisha Bhagowat

Master of Medicine: Approval of Title

We have pleasure in advising that your proposal entitled *Effect of caregiver's recorded voice on emergence delirium in children undergoing dental surgery* has been approved. Please note that any amendments to this title have to be endorsed by the Faculty's higher degrees committee and formally approved.

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

5.3 RMMCH Committee approval

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

RAHIMA MOOSA MOTHER AND CHILD HOSPITAL

RAHIMA MOOSA MOTHER AND CHILD HOSPITAL
Enquiries : Karen Marshall
Tel : (011) 470 9284
Fax : 086 553 4623
Email : Karen.Marshall@wits.ac.za

TITLE OF RESEARCH PROJECT:
"Effect of caregiver's recorded voice on emergence delirium in children undergoing dental surgery"

PRINCIPAL INVESTIGATOR:
Dr Marisha Bhagowat
Department of Anaesthesiology
Faculty of Health Sciences
University of the Witwatersrand

SUPERVISOR:
Professor Juan Scribante
Department of Anaesthesiology
Faculty of Health Sciences
University of the Witwatersrand

NHRD REF NO: GP_201905_036

Dear Dr. Bhagowat,

Permission is granted for you to conduct the research as indicated in the title above.

The terms under which this permission is granted is contained in the Researcher Declaration form that you have signed. Failure to comply with these conditions will result in the withdrawal of such permission.

It is crucial for you to inform the Research Coordinator, Karen Marshall of the actual start and end dates of your study. This could be done by e-mail.

Should the study commence more than 12 months after receipt of this approval letter you will have to go through the process of applying again.

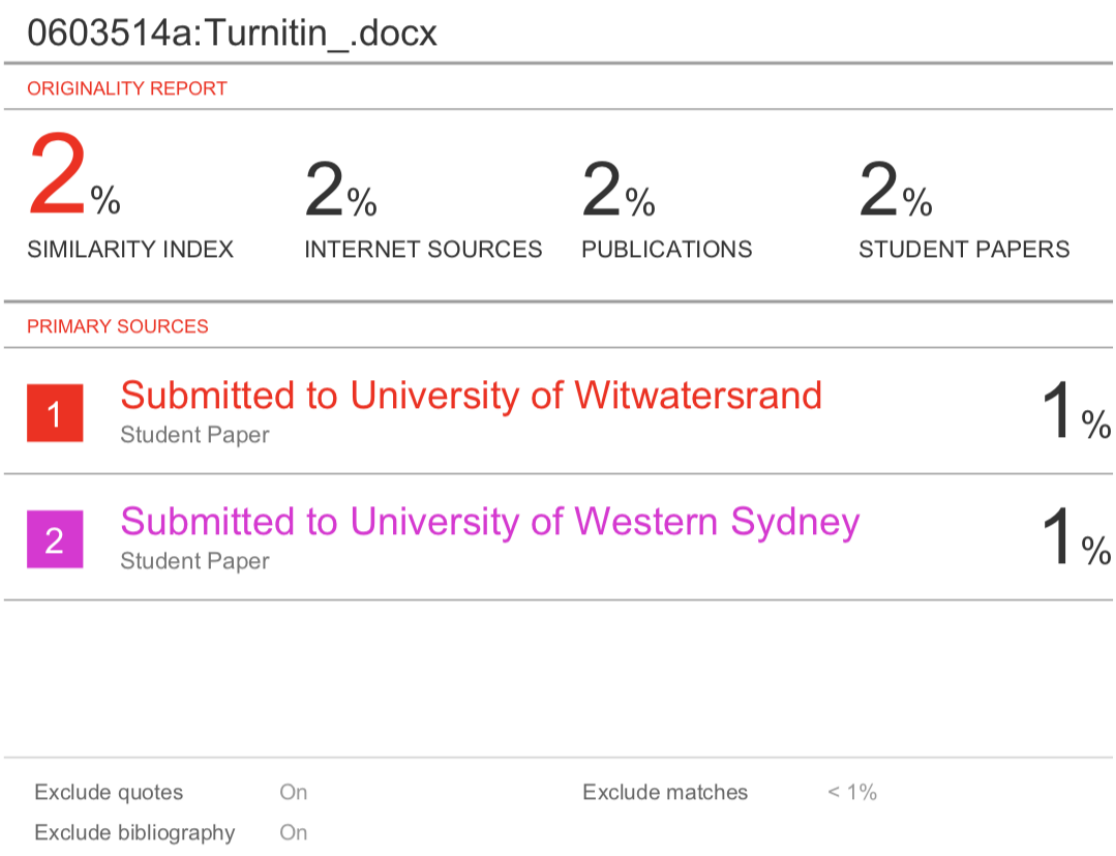
You are strongly advised to keep a signed copy of the declaration form so as to ensure that the terms of this agreement are complied with at all times.

Yours sincerely,

DR FREW BENSON
ACTING CHIEF EXECUTIVE OFFICER
2019:05:27

ADDRESS: Cnr FUEL & OUDSTHOORN STREET CORONATIONVILLE 2093 / PRIVATE BAG X20 NEWCLARE 2112 JHB

5.4 Turnitin report



0603514a:Turnitin_.docx

ORIGINALITY REPORT

2%	2%	2%	2%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Submitted to University of Witwatersrand Student Paper	1%
2	Submitted to University of Western Sydney Student Paper	1%

Exclude quotes	On	Exclude matches	< 1%
Exclude bibliography	On		

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG | FACULTY OF HEALTH SCIENCES

25 November 2019

The Chairperson
Graduate Studies Committee
Faculty of Health Sciences
University of the Witwatersrand

Dear Professor Papathanasopoulos

Re: M Med: **The effect of caregivers recorded voice on emergence delirium in children undergoing dental surgery**

Dr Marisha Bhagowat, student number: 0603514A, has submitted her research report to Turnitin which revealed a similarity index of 2%. These similarities appear not to be plagiarism but mainly the use of common terminology and phrases specific to the topic of the research.

Yours sincerely,

J. Scribante

Juan Scribante
Supervisor