# COMPARING THE EFFICACY BETWEEN DESFLURANE AND SEVOFLURANE IN MAINTENANCE OF SPONTANEOUS GENERAL ANAESTHESIA USING AMBU®AURAGAIN™ IN PAEDIATRIC PATIENTS: A RANDOMISED CONTROLLED TRIAL

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Tengku Nordiana binti Tengku Hamzah

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## LIST OF ABBREVIATIONS

| | |
|---|---|
| ANOVA | Analysis of Variance |
| ASA | American Society of Anesthesiologists |
| BMI | Body mass index |
| CI | Confidence interval |
| DBP | Diastolic blood pressure |
| ETT | Endotracheal tube |
| GA | General anaesthesia |
| HR | Heart rate |
| ICU | Intensive care unit |
| IQR | Interquartile range |
| IV | Intravenous |
| JEPeM | Jawatankuasa Etika Penyelidikan Manusia USM |
| LMA | Laryngeal mask airway |
| l/min | Litre per minute |
| MAC | Minimum alveolar concentration |
| MAP | Mean arterial pressure |
| MDI | Metered Dose Inhaler |
| µg/kg | microgram per kilogram |
| mg/kg | milligram per kilogram |
| ml/kg | millilitre per kilogram |
| NNH | number needed to harm |
| OD | odd ratio |
| PAED | Paediatric Anaesthesia Emergence Delirium scale |

| | |
|---|---|
| RCT | Randomised controlled trial |
| RR | Relative risk |
| SBP | Systolic blood pressure |
| SD | Standard Deviation |
| SMD | Standardized Mean Difference |
| SPSS | Statistical Package for the Social Sciences |
| URTI | Upper respiratory tract illness |
| USM | Universiti Sains Malaysia |

## ABSTRAK

**Latarbelakang** Proses induksi dan bangun sedar dari bius am yang pantas bagi gas desflurane mengelakkan daripada komplikasi yang dikaitkan dengan masa pembiusan am yang panjang sebelum pesakit sedar daripada bius am jika dibandingkan dengan gas sevoflurane. Walaubagaimanapun, kerana bau yang menyengat, gas desflurane tidak digunakan sebagai gas induksi untuk pembiusan am dikalangan pesakit pediatrik kerana ia boleh menyebabkan kerengsaan salur pernafasan. Tujuan kajian ini adalah untuk membandingkan hemodinamik, masa bangun sedar dari bius, bangun sedar agitasi dari bius dan komplikasi respiratori gas desflurane dibandingkan dengan gas sevoflurane bagi kelangsungan bius am dengan pernafasan spontan dikalangan pesakit pediatric menggunakan Ambu®AuraGain™.

**Kaedah** Kajian rawak ini melibatkan 80 pesakit American Society of Anesthesiologists (ASA) fizikal I yang dijadualkan untuk menjalani pembedahan elektif di bawah pembiusan am. Pesakit dibahagikan secara rawak kepada dua kumpulan; kumpulan sevoflurane (kumpulan S, $n = 40$): dan desflurane (kumpulan D, $n = 40$) sepanjang tempoh pembiusan. Kesan kedua-dua kumpulan ini ke atas hemodinamik setiap 10 minit dan respiratori sepanjang pembedahan, masa yang diambil untuk sedar daripada bius am serta agitasi selepas pembiusan akan di nilai.

**Keputusan** Masa yang diperlukan untuk sedar dari bius am selepas desflurane memakan masa yang lebih pantas berbanding dengan sevoflurane [6.92(2.47) vs 9.95(55.52), $P = 0.003$] dan kekerapan agitasi selepas pembiusan adalah lebih rendah ($P = 0.014$). Tiada perbezaan ketara ke atas perubahan hemodinamik dari segi SBP, DBP, MAP dan HR sepanjang pembedahan dan kesan sampingan ke atas respiratori sepanjang dan selepas pembedahan ($P > 0.05$ masing-masing).

**Kesimpulan** Kelangsungan pembiusan am dengan pernafasan spontan dikalangan pesakit pediatrik menggunakan gas desflurane mempunyai masa bangun sedar dari bius am yang singkat dan juga kurang kekerapan dan keterukan agitasi berbanding gas sevoflurane.

## ABSTRACT

**Background** Desflurane has a rapid onset and offset of anaesthesia, thus minimising complications associated with prolonged recovery compared to sevoflurane. Nevertheless, due to its pungency, it is avoided as induction agent in paediatric as it may cause airway irritability. This study aimed to evaluate the haemodynamic, emergence time, emergence agitation and respiratory adverse event of desflurane in comparison to sevoflurane in maintaining general anaesthesia with spontaneous breathing in paediatric population using Ambu®AuraGain™, as previous studies were done in paralysed and controlled ventilated patients.

**Methods** This study was prospective, single blinded, single centre and randomised controlled trial. A total of 80 American Society of Anaesthesiologists (ASA) physical status I children patients underwent short (1 to 2 hours) elective surgeries were randomised into two groups; sevoflurane (Group S, $n = 40$): and desflurane (Group D, $n = 40$) for maintenance of spontaneous breathing general anaesthesia. Both groups were observed for emergence time, frequency and severity of emergence agitation, the respiratory adverse events and intraoperative and post-operative haemodynamic of every 10 minutes. All data were analysed using independent *t*-test, Pearson chi-squared and repeated measures ANOVA respectively.

**Results** Emergence time was significantly shorter [6.92(2.47) vs 9.95(55.52), $P = 0.003$] with reduced frequency and severity of emergence agitation ($P = 0.014$) in desflurane group compare to sevoflurane. However, there was no significance difference in term of intraoperative haemodynamic for SBP, DBP, MAP and HR and perioperative respiratory adverse events in both groups ($P > 0.05$ respectively).

**Conclusion** Maintenance of general anaesthesia with spontaneous breathing in paediatrics using desflurane had faster emergence time with reduced frequency and severity of emergence agitation as compared to sevoflurane.

**Keywords** anaesthetics, paediatric, inhalational, desflurane, sevoflurane

# CHAPTER 1 : INTRODUCTION

## 1.1 Introduction

The conduct of anaesthesia in paediatric patients presents unique challenges. The variability of behavior and response of children at induction is one of the most striking challenges. Volatile anaesthetic agents widely used as a maintenance of general anaesthesia. Both sevoflurane and desflurane are a halogenated volatile anaesthetic agents. Desflurane has a lower blood-gas partition coefficient and lower blood-tissue partition coefficient which has a faster onset and offset of actions as compared to sevoflurane (1). Cardiovascular profile of desflurane is as safe as sevoflurane and isoflurane (2,3). Furthermore, desflurane is favourable in paediatrics due to effects of increase in heart rate and blood pressure that usually seen in adults after a high and rapid increase in desflurane concentration (4).

Sevoflurane has a sweet smell which makes it suitable agent to be used as an induction agent. Desflurane however, has a pungent smell which makes it unsuitable for induction agents as it can cause incidence of laryngospasm in 50% of patients (5)**.** This is of particular interest especially for maintenance of general anaesthesia with spontaneous breathing. This is because, the previous study in paediatric population comparing sevoflurane and desflurane as a maintenance of general anaesthesia was done in a controlled breathing situation with the usage of muscle relaxant (6).

Even though sevoflurane is widely used as an induction agent in paediatric anesthesia, its emergence behavior such as an increased emergence agitation compared to desflurane and isoflurane are the drawbacks for sevoflurane (7). With good cardiovascular profiles and lower

blood-gas partition coefficient, desflurane is seen as a suitable agent for maintenance of anaesthesia and rapid recovery (1,5) especially in paediatric population who are prone to post-operative apnoea or desaturation (4).

Hence, the aimed of this study was to establish and compare the effect of desflurane in maintenance of spontaneous breathing general anaesthesia in paediatrics as compared to sevoflurane. This study focused on the effect of desflurane on the emergence time, frequency and severity of emergence agitation, and respiratory adverse events as the primary outcome while the effects of desflurane on haemodynamic parameters (SBP, DBP, MAP, HR) as secondary outcomes.

## 1.2 Rationale of Study

Adequate maintenance of spontaneous breathing general anaesthesia is paramount as well as faster recovery profile in paediatric populations to ensure least complications from general anaesthesia. Thus, choosing the best inhalational agent is utmost important.

This study will give an overview of any statistically significant differences in terms of:

- Intraoperative haemodynamic changes
- Emergence time and agitation
- Perioperative respiratory events

## 1.3 Study Objective

### 1.3.1 General Objective

To evaluate the effectiveness of desflurane in comparison to sevoflurane in maintaining spontaneous breathing general anaesthesia in paediatrics population using Ambu ®AuraGain™.

### 1.3.2 Specific Objective

- To compare the intraoperative haemodynamic parameters (SBP, DBP, MAP and HR at every 10 minutes) between desflurane and sevoflurane in maintenance of spontaneous breathing general anaesthesia in paediatric population using Ambu ®AuraGain™.
- To compare the emergence time between desfurane and sevoflurane in maintenance of spontaneous breathing general anaesthesia in paediatric population using Ambu ®AuraGain™.
- To compare the respiratory events intraoperative and post-operative (i.e.: breath holding, bronchospasm, coughing, secretions, desaturations) between desflurane and sevoflurane in maintenance of spontaneous breathing general anaesthesia in paediatric population using Ambu ®AuraGain™.
- To compare the frequency and severity of emergence agitation between desflurane and sevoflurane.

## 1.4 Hypothesis

### 1.4.1 Null Hypothesis

1. There is no difference in haemodynamic parameters intraoperatively in patient receiving desflurane and sevoflurane.
2. There is no difference in emergence time among patients receiving desflurane and sevoflurane.
3. There is no difference among patients receiving sevoflurane and desflurane in respiratory events intraoperative and post-operative (i.e.: breath holding, bronchospasm, coughing, secretions, desaturations).
4. There is no difference in emergence agitation among patients receiving desflurane and sevoflurane.

### 1.4.2 Alternative Hypothesis

1. There are more haemodynamic parameters changes intraoperatively in patient receiving desflurane compared to sevoflurane.
2. Patients receiving desflurane has faster emergence time compared to those receiving sevoflurane.
3. There is more respiratory events intraoperative and post-operative (i.e.: breath holding, bronchospasm, coughing, secretions, desaturations) in patients receiving desflurane compared to sevoflurane.
4. There is lesser emergence agitation severity among patients receiving desflurane compared to sevoflurane.

## 1.5 Literature Review

Sevoflurane and desflurane are volatile anaesthetic agents with low blood gas solubility (0.65 vs 0.45) ensures rapid onset of anaesthesia (induction) and offset (emergence) (1). Cardiovascular profile of desflurane is as safe as sevoflurane and isoflurane (2). Also, desflurane is favourable in paediatrics due to effects of increase in heart rate and blood pressure that usually seen in adults after a high and rapid increase in desflurane concentration (2).

Nevertheless, desflurane has drawback which it can caused airway irritability due to its pungency, such as coughing, breath holding, laryngospasm and copious secretions, therefore it is not used as inhalational induction of anaesthesia in paediatrics. A landmark study by Lerman et al (3) used by the desflurane manufacturer as a reference, compared airway responses to desflurane and isoflurane on paediatrics population using LMAs and facemask, concluded that the frequency of major airway events after desflurane (9%) was similar to that after isoflurane (4%) (Number Needed to Harm, NNH 20). However, there was a higher incidence of respiratory events (e.g. coughing, laryngospasm, secretions) in patients with desflurane maintenance anaesthesia if the LMAs were removed during deep desflurane anaesthesia (15%) than awake removal (5%) ($P < 0.006$) and deep desflurane anaesthesia removal (15%) greater than deep isoflurane anaesthesia LMAs removal (2%) ($P < 0.03$)(NNH of 8). The frequency of airway events of any severity was also higher in desflurane group compared to isoflurane (39% vs 27%) ($P < 0.05$). However this study has several drawbacks; the desflurane group was randomised three times more than isoflurane group which as a consequence of unbalanced study design the frequency of airway events in isoflurane group might have been underestimated. The anaesthetic agent was the only variable that been randomised, the type of airway, anaesthesia depth for airway removal were not randomised in this study. A retrospective study done by No HJ et al (4) which compared perioperative respiratory events

using either desflurane or sevoflurane in paediatrics underwent general anaesthesia via supraglottic airway as maintenance of anaesthesia showed that the incidence of upper airway respiratory events in 3439 evaluated patients was 0.43% (12/2777) in sevoflurane group and 0.30% (2/662) in the desflurane group $P = 0.75$; Odds Ratio, OR = 0.69% (95% Confidence Interval, CI: 0.63,3.13). The difference between this two groups was not significant which concluded that compared with sevoflurane, desflurane did not increase the risk of perioperative upper airway events in paediatrics receiving general anaesthesia via a supraglottic airway. Considering these conflicting findings, there is a need to further investigate on this.

A study done by Satyanarayana et al (5), which compared airway responses, haemodynamic and recovery following sevoflurane and desflurane in paediatrics day care surgeries concluded that haemodynamic parameters in both groups showed no statistically difference. Kotwani et al (6) did a comparison of maintenance, emergence and recovery characteristics of sevoflurane and desflurane in paediatrics ambulatory anaesthesia. Intraoperative haemodynamic between the 2 groups were comparable, which maintained within ±20% of baseline values.

Another aspect of interest was the effect of desflurane on emergence agitation in paediatric population. Even though desflurane allow faster recovery, it showed to cause emergence agitation which were reduced with the administration of dexmedetomidine (7). Moreover, newer less soluble volatile agent such as sevoflurane and desflurane had higher incidence of emergence agitation as compared to halothane (more soluble agent) and propofol (intravenous agent) (8). However, in another study, the incidence of emergence agitation in both sevoflurane and desflurane were comparable (10% in group sevoflurane, 16.7% in group desflurane) with $P = 0.226$ (6). Meta-analysis of 158 studies involving 14 045 children showed

that there's no clear evidence that desflurane had increased risk for emergence agitation compared to sevoflurane [Relative Risk, RR 1.46, (95% Confidence Interval, CI: 0.92 ,2.31), moderate quality of evidence] (9). Systematic review and meta-analysis of the incidence and severity of emergence agitation were comparable between desflurane and sevoflurane in paediatrics patients [RR = 1.21; (95% CI: 0.96,1.53)] for incidence and Standardized Mean Difference, SMD = 0.12; (95% CI: -0.02,0.27) for severity(3). Emergence characteristic were shorter in desflurane group of anaesthesia ($P < 0.001$) with recovery time needed for desflurane group was 40% shorter (18±8.3min) than sevoflurane group (45±9.7min) (6).

Supraglottic airway devices are routinely used in modern anaesthesia. The latest supraglottic device in paediatrics have additional safety feature such as gastric access port. Ambu ®AuraGain ™, is a cuffed supraglottic airway which has a curved and integrated gastric access with a wide airway tube which allows as a conduit in tracheal intubation. To improve its fit it has less rigid airway tube and mask. A randomised trial comparing the Ambu®AuraGain™ and the LMA®supreme in infants and children for airway maintenance during mechanical ventilation showed that the ease, time and success rate for device placement, gastric tube insertion and complications were not significantly different (10). Paediatrics patients which received LMA supreme required more airway manoeuvres (7 vs 1 patient, $P = 0.06$) to maintain patent airway.

# CHAPTER 2 :

# BODY OF MANUSCRIPT

## 2.1 Title page

### 2.1.1 Article Title

**THE EFFICACY OF DESFLURANE AND SEVOFLURANE AS A MAINTENANCE OF SPONTANEOUS BREATHING GENERAL ANAESTHESIA IN PAEDIATRICS**

### 2.1.2 Running Head

Efficacy between Desflurane vs Sevoflurane

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## 2.2 Main Documents

### 2.2.1 Title

**THE EFFICACY OF DESFLURANE AND SEVOFLURANE AS A MAINTENANCE OF SPONTANEOUS BREATHING GENERAL ANAESTHESIA IN PAEDIATRICS : A RANDOMISED CONTROLLED TRIAL**

### 2.2.2 Abstract

**Background** Desflurane has a rapid onset and offset of anaesthesia, thus minimising complications associated with prolonged recovery as compared to sevoflurane. Nevertheless, due to its pungency, desflurane is avoided as induction agent in paediatric as it may cause airway irritability. This study aimed to evaluate the haemodynamic, emergence time, emergence agitation and respiratory adverse event of desflurane in comparison to sevoflurane in maintaining general anaesthesia with spontaneous breathing in paediatric population using Ambu®AuraGain™.

**Methods** This study was a prospective, single blinded, single centre and randomised controlled trial. A total of 80 American Society of Anaesthesiologists (ASA) physical status I paediatric patients for short duration elective surgery were randomised into two groups; sevoflurane (Group S, $n$ = 40): and desflurane (Group D, $n$ = 40) for maintenance of spontaneous breathing general anaesthesia. Both groups were observed for emergence time, frequency

and severity of emergence agitation, the respiratory adverse events and intraoperative and post-operative haemodynamic of every 10 minutes. All data were analysed using independent *t*-test, Pearson chi-squared test and repeated measures ANOVA respectively.

**Results** Emergence time was significantly shorter [6.92(2.47) vs 9.95(55.52), $P = 0.003$] with reduced frequency and severity of emergence agitation ($P = 0.014$) in desflurane group compare to sevoflurane. Desflurane group had shorter emergence time compare to sevoflurane group by mean difference of 3.03 (95% CI: 1.13, 4.94). However, there was no significance difference in term of intraoperative haemodynamic for SBP, DBP, MAP and HR and perioperative respiratory adverse events in both groups ($P > 0.05$ respectively).

**Conclusion** Maintenance of general anaesthesia with spontaneous breathing in paediatrics using desflurane had faster emergence time with less frequency and severity of emergence agitation as compared to sevoflurane.

**Keywords** anaesthetics, paediatric, inhalational, desflurane, sevoflurane

(273 words)