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Research Article

Comparison of Depth of Anesthesia after Induction with Sodium Thiopental and Etomidate using Bispectral Index Spectrum (Bis) and Hemodynamic conditions for Uncooperative Children undergoing Dental Treatment

Nasser Kaviani[1] and Arezoo Mahdian[2*]

[1]assistant Professor, Anaesthesiologist, Oral And Maxillofacial Department
And Dental Reserch Center, Dental School, Isfahan University Of Medical Sciences, Isfahan, Iran.
[2]Postgraduate Student, Department of Orthodontics, School of Dentistry,
Shahid Beheshti University of Medical Sciences, Tehran, Iran.
[*]Corresponding author:E-mail: arezo_mahdiaan@yahoo.comphone: +989129052759

ABSTRACT

Introduction: Etomidate has been used to induce anesthesia with minimal changes in hemodynamic profile in many inductions of general anesthesia. Since etomidate increases the brain activity and it seems that the patient is in higher level of consciousness, this study was designed to compare anesthetic depth of etomidate and thiopental.

Material and methods: This double-blinded prospective randomized controlled trial was performed on two groups of 17 children who underwent general anesthesia. One group was induced by thiopental and another group was induced by etomidate. Depth of anesthesia by BIS, mean arterial blood pressure and oxygen saturation were measured before, immediately after and 5 minutes after intubation and the incidence of nausea and degree of agitation in the recovery room were recorded. Independent t-test, paired t-test, Mann-Whitney analyze, chi square analyzed, fisher exact test and variance analyze for repeated data were used to analyze the data (α=0.05).

Results: Age and gender were similar between the two groups. BIS, SPO_2 and mean arterial blood pressure before, immediately after and 5 minutes after intubation and the incidence of nausea and degree of agitation in recovery in the etomidate group had no significant difference with thiopental.

Conclusion: Etomidate has similar depth of anesthesia and hemodynamic effects with thiopental and has no significant adverse effect in recovery time. Therefore, etomidate can be used safely as an alternative of thiopental when thiopental is not available or is not indicated for any reason.

Key words: BIS, Etomidate, Thiopental Sodium, General anesthesia

[I]INTRODUCTION

Patient cooperation is of great importance for dental treatment and, if failed, can make it difficult to treat and reduce the quality of treatment. On the other hand, medical emergencies such as foreign body aspiration are more likely to occur when the child is crying or there is the risk of oral and facial injury (1).

Sometimes the efficient, effective and safe treatment of children requires the use of general anesthesia (GA) in dentistry (2). The main purpose of general anesthesia is to prevent the patient from feeling the pain that occurs during surgery and provide comfort and anesthesia so that the patient does not remember anything about surgery. However, if judgments of depth of anesthesia are not precise, it leads to awakening during the operation (3).Induction agents are essential components of rapid sequence intubation and cause amnesia, repression of sympathetic responses and better intubation conditions. Propofol is the most widely used anesthetic agent for induction of anesthesia and intubation, with

the complication of high blood pressure (4). In addition, other anesthetic agents, such as sodium thiopental and midazolam, cause a drop in blood pressure. In this regard, the hemodynamic stability and minimal cardiovascular effects associated with etomidate have made the drug more attractive as an anesthesia induction agent (5, 6). It has no analgesic properties and minimal hemodynamic effects.

Having a standard induction dose of 0.2-0.6 mg/kg, etomidate is used as effective as propofol and thiopental at the beginning of anesthesia. It can increase cerebral activity and is associated with grand mal seizures (7). In a study of children with a mean age of 4 years in 2012, Lin *et al.* (8) showed that children need higher doses of etomidate than adults for induction. A study by Zuckerbraun*et al.* (9), performed in children with a mean age of 8.2 (±6.2) years in 2006, showed no significant hemodynamic changes after successful induction with etomidate. In 2003, Lallemand*et al.* (10) examined the physical characteristics of 30 patients at three different doses of etomidate at an appropriate depth of anesthesia (assessed by BIS) and found no statistically significant difference between the two groups of patients with respect to the loss of eyelash reflex, the time to a decrease in BIS to 50, and the time to a decrease in BIS to 30 after intubation and plasma concentrations of etomidate. HR and mean arterial pressure were increased but not significantly different between the two groups. No awakening and consciousness occurred during surgery in the groups.

Bispectral index spectrum (BIS) is a non-invasive technology that provides a clinical evaluation of depth of anesthesia (11, 12). It also provides clinicians with unique information about the appropriate doses of hypnotic drugs to address the needs of individual patients (13). Decrease in consciousness level is a common reason for intubation using the anesthesia induction drug so as not to feel pain and remember the painful memories of this stage.Since etomidate increases cerebral activity and seizure-like attacks and the patient appears to have a higher level of consciousness during induction of anesthesia, we intended to measure the depth of anesthesia induced by the drug using BIS and compare it with sodium thiopental - a common medication for induction of anesthesia - to ensure that the desired anesthetic depth is achieved by changing the dose, if necessary.

[II] MATERIALS AND METHODS

In this prospective, single-blind clinical trial, we chose 34 healthy, distressed and uncooperative children aged 3-5 years who were referred to the operating room of the Faculty of Dentistry at Isfahan University of Medical Sciences for dental treatment under GA and who met the inclusion criteria. Inclusion criteria are age 3-5 years, being uncooperative with a Frankl score of 1 or 2 (negative), lack of special disease (ASA I), being referred for dental treatment under GA, no prohibition on the use of anesthesia, no prohibition to use thiopental and etomidate, and the absence of common cold symptoms at surgery. There are certain exclusion criteria, including specific medical problems during the operation, an allergy to drugs given, the use of additional drugs during the induction of anesthesia, and the anesthesiologist's inability to perform nasotracheal intubation for various reasons.

Patients were asked to refer for a surgery (in fasting state, at least NPO 4 hours) that was going to be performed in the morning.Before the start of the study, written informed consent was received from the legal guardian of each patient entered into the study. On the morning of surgery, each patient was given a code of which only the anesthesiologist, and no others researchers, was aware. Then, the anesthesiologist randomly divided the patients into two groups based on odd or even codes. Before proceeding with any surgery, the BIS VISTA monitor (Vista Monitoring System Co., USA) was used with a special lead for children (ASPECT medical system Co., USA) to measure and record the baseline levels of consciousness in both groups.

Etomidate (0.4 mg/kg), fentanyl (2µg/kg, as an opioid analgesic) and atracorium (0.6 mg/kg/min)

were administered intravenously in the group with odd codes, while the group with even codes received sodium thiopental (at a dose of 3 mg/kg), fentanyl (at a dose of 2 µg/kg, as an opioid analgesic) and atracorium (at a dose of 0.6 mg/kg/min). After induction and before intubation, we measured and recorded the depth of anesthesia by the BIS monitor, and mean arterial blood pressure and blood oxygen saturation levels by the vital signs monitor (Cardioset FX7 monitoring, Sairanmed Co., Isfahan, Iran). Then, nasotracheal intubation was performed by the anesthesiologist.The BIS scores, mean arterial blood pressure and blood oxygen saturation percentage were measured and recorded immediately and five minutes after intubation. Oxygen 50%, nitrous oxide 50% and propofol at a dose of 100 mg/kg/min were used after intubation in both groups to maintain anesthesia. After surgery, the patient was transferred to the recovery room and the incidence of nausea was recorded in both groups. The agitation occurring during recovery was recorded by the Pediatric Anesthesia Emergence Delirium Scale (Sikich and Lerman 2004) (Appendix 1) (11). Measurement and monitoring of nausea severity was based on the clinical judgment of the anesthesiologist.

After having met the discharge criteria designated by the Post Anesthesia Discharge Scoring System (PADS) (Appendix 2), the patient was discharged following a full consultation in which the patient's legal guardian gave a contact telephone number. The codes were opened after sample collection, and then the information entered into computer systems were analyzed by the Statistical Package for the Social Sciences (SPSS) (22nd version). The data collected in this study were also analyzed using the independent t-test, paired t-test, Mann-Whitney test, Chi-square test, Fisher's exact test and ANOVA for repeated data (α=0.05).

[III] RESULTS

None of the 34 children eligible for study were excluded from the study. This study was performed in two groups of 17 children. Sex and age profile of patients in both groups were similar (Table 1).

Table 1: Sex and age profile of patients

Group	The average age	Girl	Boy
Sodium Thiopental	3.94 (±0.68)	9	8
Etomidate	3.85 (±0.7)	7	10
P value	0.713	0.492	

The number of people ranked by the Frankel score of -1 and -2 (in terms of cooperation) was 5 and 12 people in the thiopental group and 6 people and 11 people in the etomidate group, respectively.

The mean BIS values in the two etomidate and sodium thiopental groups were not significantly different before and after anesthetic administration as well as before, immediately after, and five minutes after intubation (Table 2 and figure 1).

Table 2: The mean (± SD) BIS at different times

Group	before anesthetic administration	after anesthetic administration	immediately after intubation	five minutes after intubation
Sodium Thiopental	98.76(±1.2)	47.82(±4.95)	53.76(±3.99)	44.23(±3.53)
Etomidate	98.64 (±1.16)	49.88 (±5.03)	55.7 (±6.76)	46.11(±5.36)
P value	0.774	0.238	0.316	0.314

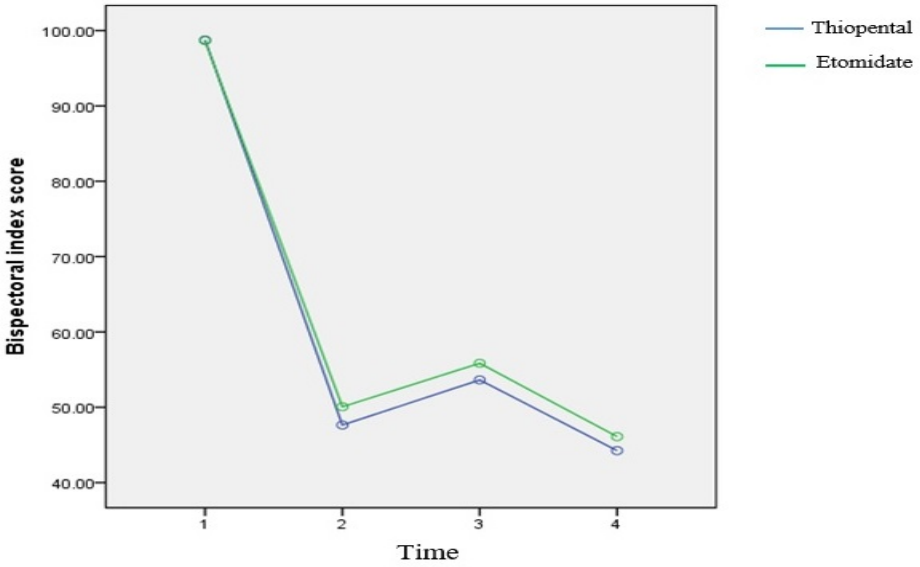

Figure 1: The mean BIS at different times

1. before anesthetic administration
2. after anesthetic administration
3. immediately after intubation
4. Five minutes after intubation Five minutes after intubation

The mean values of SPO2 before, immediately after and five minutes after intubation were not significantly different between the two groups (Table 3 and figure 2).

Table 3: The mean (± SD) SPO_2 at different times

Group	Before intubation	Immediately after intubation	Five minutes after intubation
Sodium Thiopental	97.71 (±0.772)	99.35 (±00.772)	99.24 (±0.664)
Etomidate	97.59 (±0.871)	99.24 (±0.831)	99.29(±0.686)
P value	0.679	0.659	0.801

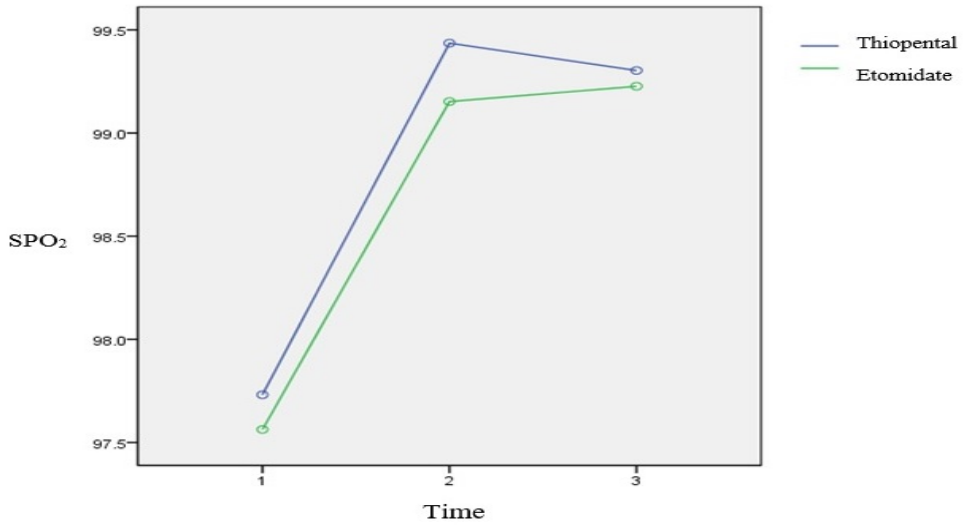

Figure 2: The mean SPO_2 at different times

1. Before intubation
2. Immediately after intubation
3. Five minutes after intubation

No significant difference in mean arterial blood pressure was found between the two groups before, immediately after, and five minutes after intubation (Table 4 and figure 3).

Table 4: The mean (± SD) arterial blood pressure at different times

Group	Before intubation	Immediately after intubation	Five minutes after intubation
Sodium Thiopental	5.95 (±0.131)	6.06 (±0.184)	5.76 (±0.225)
Etomidate	5.87 (±0.225)	6 (±0.221)	5.75(±0.251)
P value	0.2	0.363	0.808

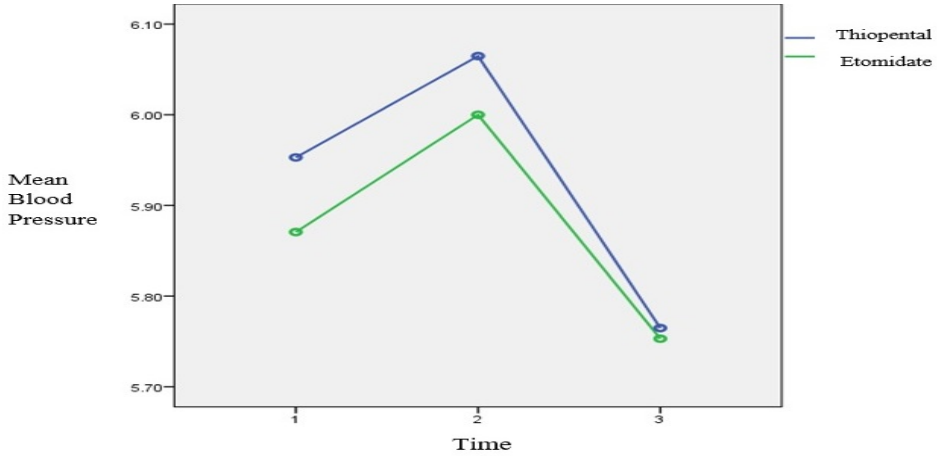

Figure 3: The mean (± SD) arterial blood pressure at different times

1. Before intubation
2. Immediately after intubation
3. Five minutes after intubation

In the thiopental group, 16 patients had no nausea and 1 patient had mild nausea at the time of recovery, while in the etomidate group, there were 15 patients without nausea, 1 patient with mild nausea and 1 patient with moderate nausea. Thus, there was no significant difference in the incidence of nausea between the two groups (P value=0.76) (Table 5). However, no significant difference in the incidence of agitation was found between the two groups (Table 6).

Table 5: The frequency of nausea during recovery

	nausea			
Group	-	mild	moderate	severe
Sodium Thiopental	16	1		0
Etomidate	15	1	1	0
P Value	0.76			

Table 6: Frequency of agitation during recovery timein degrees

	AgitationIn degrees											
Group	1	2	3	4	5	6	7	8	9	10	11	12
Sodium Thiopental	0	2	0	4	2	3	0	3	1	0	1	1
Etomidate	0	1	0	1	4	5	0	3	1	2	0	0
P value	0.553											

ANOVA for repeated data showed a statistically significant difference between the mean BIS values at different times (P value<0.001) but no significant difference between the two etomidate and thiopental groups (P value=0.153). The interaction between the groups was not significant (0.920), meaning no significant difference between the two groups at different times.

[IV] DISCUSSION

The results of this study confirm the null hypothesis and there was no significant difference in the anesthetic depth of the two etomidate and thiopental drugs.BIS is a good reliable indicator to assess the depth of anesthesia for all anesthetics and can be used to titrate the dose of anesthetic in all phases of anesthesia. A BIS value between 40 and 60 indicates an active and awake central nervous system, while zero indicates an isoelectric EEG. BIS values between 70 and 90 indicate loss of consciousness and sedation, whereas a BIS score of 60 and <40 indicates light anesthesia and deep anesthesia, respectively. BIS values between 40 and 60 were reported to provide an adequate depth of anesthesia for GA and surgery (15). As the results of this study show, the BIS value of the group induced with etomidate is higher than that of the thiopental group in all the processes and increases in both the groups during intubation, and the increasing and decreasing pattern of the indicator is similar in both groups. However, the difference between the two groups was not statistically significant at any of the measurement times.During the time of intubation, both groups showed the highest BIS levels of 53.79 (±3.99) and 55.7 (±6.76) in the sodium thiopental and etomidate groups, respectively (P value =0.316). Since no significant difference in anesthetic depth was observed between the etomidate and thiopental groups, the BIS value (and thus the level of consciousness) in the etomidate group is not too higher that the patient is brought out of anesthesia and can realize the events in the surrounding environment and the pain associated with intubation. Consistent with our study, Lallemand*et al.* (10) who examined different doses of etomidate in 2003 found no consciousness and awakening at any dose in patients undergoing dental treatment.

For the three measurement times, mean arterial blood pressure in the etomidate group was lower than that in thiopental group. However, they were much closer together five minutes after intubation. In addition, the pressure increased during intubation in both groups, but to a lesser extent in the etomidate group. The difference between the two groups was not statistically significant in this regard.This result is consistent with the study of Habibi*et al.* (16) who compared the hemodynamic effects of etomidate versus ketamine-thiopental in 2014. In a study to measure the mean systolic and diastolic blood pressure in 2013, Agha Davoodi*et al.* (17) found no significant difference between in the group sedated with etomidate and the group sedated with ketamine, fentanyl and midazolam. Consistent with our study, Glunder*et al.* (18) in 2002 showed that etomidate can increase the mean systolic and diastolic blood pressure as compared to the initial measurement.The results of our study are inconsistent with the results of a study by Petrun*et al.* (19) who compared the hemodynamic effects of etomidate versus propofol in 2013 and found that mean arterial pressure was substantially higher than that of the etomidate group at the time of intubation and thereafter seven minutes after intubation. This difference may be due to the difference between the compared drug and etomidate. In a study aimed to compare etomidate versus propofol in 2015, Kaushal*et al.* (20) found a loss of arterial pressure in propofol and a more hemodynamic stability in etomidate.In a study examining the mean arterial pressure at different doses of etomidate in 2003, Lallemand*et al.* (10) concluded that although etomidate can increase arterial blood pressure, there is no significant difference between the doses. In addition, oxygen saturation in the etomidate group was lower than that in the thiopental group at all times studied and increased with the same pattern during intubation in both groups. Five minutes after intubation, the SpO2 value, however, decreased in the thiopental group and increased in the etomidate group, although this change was not statistically significant. This result is consistent with the results of Mousavi who compared etomidate versus propofol in 2012 (21).

No statistically significant difference in the incidence of nausea was observed between the etomidate and sodium thiopental groups at the

time of recovery, which is consistent with the results of Agha Davoodi*et al.* (22) in 2012. In this study, no difference in the incidence of nausea was observed between the two etomidate-fentanyl and ketamine-midazolam groups. In addition, Agha Davoodi*et al.* (17) found the same result in another study to compare ketamine-midazolam-fentanyl versus etomidate in 2013. In a study of children under 10 years of age, Glunder*et al.* (18) found that nausea is not a common complication after induction of anesthesia with etomidate.Since no statistically significant difference in the degree of agitation was observed between the two groups at the time of recovery, it does not give etomidate a special advantage over thiopental.

[V] CONCLUSION

As an anesthetic induction agent, etomidate provides a depth of anesthesia and hemodynamic effects similar to those obtained with thiopental in children aged 3-5 years, with no clinically significant side effects at the time of recovery. Accordingly, etomidate can be safely used instead of thiopental in cases where sodium thiopental is not available for induction and/or, for any reason, there is a contraindication for the use of this drug. A similar study is recommended to be performed at different doses of etomidate for different age groups to compare with other drugs used for induction of anesthesia.

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Appendix 1: Agitation scoring system during recovery

Pediatric Anesthesia Emergence Delirium scale Sikich and Lerman 2004/ Agitation during recovery	
The child makes eye contact w*ith* caregiver	1
The child's actions are purposeful	2
The child is aware of his/her surroundings	3
The child is restless	4
the child is inconsolable	5
Items 1, 2 and 3 reverse and scoring are as follows	
not at all	4
Slightly	3
much	2
Too much	1
unlimited	0
Items 4 and 5 scores are as follows	
Not at all	0
slightly	1
much	2
Too much	3
unlimited	4

Appendix 2: The Post Anesthesia Discharge Scoring System (PADS)

Variables	Score
Vital signs	
20% of the level before anesthesia	2
20 to 40% of the level before anesthesia	1
40% of the level before anesthesia	0
Motility	
Firm walking	2
Need help	1
Inability to walk	0
nausea and vomiting	
The lowest possible	2
moderate	1
Severe	0
pain	
The lowest possible	2
moderate	1
severe	0
Surgical site bleeding	
The lowest possible	2
moderate	1
severe	0