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ORIGINAL RESEARCH

Rectal Thiopental versus Intramuscular Ketamine in Pediatric Procedural Sedation and Analgesia; a Randomized Clinical Trial

Reza Azizkhani, Mehrdad Esmailian, Azadeh shojaei*, Keihan Golshani

Department of Emergency Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

*Corresponding Author: Azadeh shojaei; Department of Emergency Medicine, Al-Zahra Hospital, Soffeh Blvd, Isfahan, Iran.
Tel: +989136470851; Fax: +983117923445; Email: dr.shojaeiazadeh@yahoo.com
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Abstract

Introduction: Physicians frequently deal with procedures which require sedation of pediatric patients. Laceration repair is one of them. No study has been performed regarding the comparison between induction of sedation with sodium thiopental and ketamine in laceration repair. Therefore, the present study was aimed to comparison of induced sedation by rectal sodium thiopental and muscular injection of hydrochloride ketamine in pediatric patients need laceration repair. **Methods:** The presented study is a single-blinded clinical trial performed through 2013 to 2014 in Ayatollah Kashani and Alzahra Hospitals, Isfahan, Iran. Patients from 3 months to 14 years, needed sedation for laceration repair, were entered. Patients were sequentially evaluated and randomly categorized in two groups of hydrochloride ketamine with dose of 2-4 milligram per kilogram and sodium thiopental with dose of 25 milligram per kilogram. Demographic data and vital signs before drug administration and after induction of sedation, Ramsey score, time to onset of action, and sedation recovery time were evaluated. Chi-squared, Mann-Whitney, and Non-parametric analysis of covariance tests were used. P<0.05 was considered as a significant level. **Results:** In this study 60 pediatric patients were entered. 30 patients with mean age of 42.8±18.82 months were received sodium thiopental and the rest with mean age of 30.08±16.88 months given ketamine. Mann-Whitney test was showed that time to onset of action in sodium thiopental group (28.23±5.18 minutes) was significantly higher than ketamine (7.77±4.13 minutes), (p<0.001). The sedation recovery time in ketamine group (29.83±7.70) was higher than sodium thiopental. Depth of sedation had no significant difference between two groups based on Ramsey score (p=0.87). No significant difference was seen between two groups in the respiratory rate (df=1, 58; F=0.002; P=0.96) and heart rate (df=1, 58; F=0.98; P=0.33). However, arterial oxygen saturation level (df=1, 58; F=6.58; P=0.013) was significantly higher in ketamine group. **Conclusion:** The findings of the present study show that Although the recovery time from sedation by ketamine is more than sodium thiopental, it's fast-acting function without effecting on the oxygen saturation level causes that ketamine is considered as the better choice for induction of sedation in pediatric patients need laceration repair. In addition, long-term effect of ketamine provides more time for the physician to do the procedure and this issue decreases the need probability to the repeated-dose. However, effectiveness of both drugs to decrease the agitation was equal, based on the Ramsey score.

Key words: Hypnotics and sedatives; barbiturates; thiopental; ketamine

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Introduction:

Physicians frequently deal with procedures which require sedation of pediatric patients. These procedures include a range from painless interventions like imaging to painful therapeutic interventions such as reduction of fracture, laceration repair, bone marrow aspiration, and central catheter insertion (1, 2). Also, presenting in unfamiliar places as operation room, unpleasant odor, performing of painful techniques, and etc. all cause to increase the mental stress, restlessness, and agitation of the children as well as lack of their cooperation with medical staffs. These reactions not only intervene with performing required therapies, but also lead to some changes in physiologic parameters such as blood pressure, heart rate, and respiratory rate (3, 4). So, choosing the right medication has a critical role in such cases.

An appropriate sedative drug causes to reduce the

needed dosage and increase the safety of procedure (5). Many of these drugs have different routes of administration and choosing the best one is varied based on the type of procedure, pain level, depth of sedation required, and patient's status (1, 6, 7). Laceration repair is one of the procedures in which addition to painfulness, the child suffer from a high agitation and stress. Thus, in such situations a procedural sedation and analgesia should be used (1, 7). Several drugs have been suggested to this purpose, while each of them has some side effects that limit their use in different clinical conditions. These side effects have a wide range from cardiovascular and respiratory systems to kidney and central nervous system. In addition, the main routes of administration of these drugs are intravenous that lead to some difficulties for using them in children (8, 9). Ketamine is one of the sedative drugs which has been used in pediatric patients for a long time. It has both sedative and analgesic features based on which it can be solitary used for painful procedures. Ketamine has been suggested as a sedative premedication in pediatric patients and recognized as a safe drug which has minimum side effects on cardiovascular and respiratory systems. Ketamine cause the lidocaine injection and suture handling to be well-tolerated for children in conditions which laceration repair is needed (10). However, some side effects when used by intramuscular route, such as delayed recovery from sedation cause to use it cautiously (11).

Sodium thiopental, as a rapid-onset short-acting barbiturate general anesthetic, is another sedative drug applied for pediatric patients. This drug is in the list of essential drugs in each therapeutic center, declared by world health organization (WHO) (12). Although it's cardiovascular and respiratory side effects are more than ketamine, it has rapid recovery from sedation (13). However, no study has been performed regarding the comparison between induction of sedation with sodium thiopental and ketamine in laceration repair. Therefore, the present study was aimed to comparison of induced sedation by rectal sodium thiopental and muscular injection of hydrochloride ketamine in pediatric patients need laceration repair.

Methods:

Study design and setting

The presented study is a randomized single-blind clinical trial performed through October 2013 to June 2014 in Ayatollah Kashani and Alzahra Hospitals, Isfahan, Iran. The study protocol was confirmed by Ethical Committee of Esfahan University of Medical Sciences. All researches observed Helsinki protocol during their assessments and drug administration. The written informed consent was given from parents of children. The study was registered in Iranian registry of clinical trial (IRCT number: IRCT2015043012072N4).

Subject

In this research pediatric patients, from 3 months to 14 years, needed sedation for laceration repair were entered. Exclusion criteria were sensitivity to sodium thiopental or barbiturates, persistent asthma, severe cardiovascular disease, porphyria, contraindications to the use of rectal medications (inflammatory, hemorrhagic, and neoplastic lesions in the intestine), children with airway infection, coronary artery disease, head trauma, eye trauma, central nervous system disease, any contraindications to receive sedation, and lack of parents' consent. Also, each event causes to stopping the procedure and lacking of response to rectal sodium thiopental administration, with maximum dose of 40 mg/kg, led to exclude the subject, too. Patients are sequentially allocated and with considering the minimum and maximum of standard deviation 15 and 3 minutes for persisting of sedation, α=0.05 and β=0.1, and the maximum error of 1.5 minutes (d=1.5), about 28 subjects were appropriate in each group (1, 7, 12).

Therapeutic intervention

Patients were randomly categorized in two groups of hydrochloride ketamine with dose of 2-4 milligram per kilogram (mg/kg) (dissolved in 10 milliliter of distilled water for muscular administration) and sodium thiopental with dose of 25 mg/kg, maximum dose of 1 gram for each child, (dissolved in 10 milliliter of distilled water for rectal administration). Randomization was done as permuted-block randomization using computerized software. Drugs were purchased from Rotexmedia Company (Germany). Because of difference routes of administration for these two drugs, it was not possible to do the study as double-blind. Thus, the administering researcher was aware from the type of drug. To remove examiner bias, data was gathered by another researcher who was blind to the group of drug administration. For suture handling, lidocaine (3-5 mg/kg of body weight as local injection) without bicarbonate and epinephrine was used to relieve the pain. The drugs were injected when arterial oxygen saturation was above 95%. In case of any drop in oxygen saturation, nasal cannula and oxygen therapy masks were used to delivery of 100% oxygen. In presenting of ketamine side effects, midazolam with dose of 0.05 mg/kg of body weight was used (dissolved in 5 milliliter distilled water as intravenous for 2 minutes).

Variables

Ramsey score was applied to assess the induced sedation. Its scale is distributed from 1 (restless and agitation in the patient) to 6 (lacking of any response) (14). The aim of induced sedation was reaching to the score of 4 (brisk response of the subject to light glabella tap or loud auditory stimulus). The time to onset of action (from administration to reach the Ramsey score of 4) and seda-

tion recovery time (from Ramsey score 4 to full consciousness of the child) were assessed. Furthermore, demographic data (age, gender), vital signs (respiratory rate, heart rate, and arterial oxygen saturation level) before drug administration and after induction of sedation (reaching to Ramsey score of 4) were also evaluated. At the end, the presence of any side effect related to the administration of assessed drugs was recorded.

Statistical analysis

Data were entered to SPSS version 21.0. Quantitative variables were presented as mean and standard deviation and qualitative ones as frequency and percentage. To assess the difference between two studied groups regarding demographic and clinical factors before therapeutic intervention Chi-squared test (for nominal qualitative variables) and Mann-Whitney test (for quantitative and ordered variables) were used. The comparison of these groups for time to onset of action and sedation recovery time, Mann-Whitney test was applied, too. Since vital signs of pediatric patients before drug administration in two groups had significant difference, nonparametric analysis of covariance test was applied to compare such factors after the administration. In all analysis $p<0.05$ was considered as a significant level.

Results:

In this study 60 pediatric patients were entered. 30 patients were received sodium thiopental and the rest ketamine. The mean age of children given sodium thiopental was 42.8±18.8 months and those received ketamine 30.10±16.88 months (p=0.01). 20 (66.7%) of patients in sodium thiopental group and 19 (63.3%) ones in ketamine group were male (p=0.79). The demographic and clinical variables of the patients is shown in Table 1. In evaluating the vital signs of patients before therapeutic intervention, it was determined that respiratory rate (p<0.001), heart rate (p<0.001), and arterial oxygen saturation level (p<0.001) were higher in ketamine group (Table 1). The time to onset of action in ketamine group was 7.77±4.13 minutes and in sodium thiopental 28.23±5.18 minutes (p<0.001). However, the sedation recovery time in ketamine group (29.83±7.70) was higher than sodium thiopental (12.57±2.57), (p<0.001). However, the depth of sedation based on Ramsey score, has no significant difference between two groups (p=0.87). In evaluating vital signs after therapeutic intervention, no significant difference was seen between two groups in the respiratory rate (df=1, 58; F=0.002; P=0.96) and heart rate (df=1, 58; F=0.98; P=0.33). However, arterial oxygen saturation level (df=1, 58; F=6.58; P=0.013) was significantly higher in ketamine group (Table 2). Moreover, no side effect related to the administration of drugs was observed until discharging the patients.

Discussion:

The findings of the present study show that the time to onset of action of sodium thiopental is significantly higher than hydrochloride ketamine, while its sedation recovery time is shorter. It is worth noting that the average of arterial oxygen saturation level in ketamine group was more than sodium thiopental (about 4%). As the result, although recovery time from ketamine sedation is more than sodium thiopental, it is considered as the better choice for induction of sedation in pediatric patients need laceration repair. In addition, long-term effect of ketamine provides more time for the physician to do the procedure and may reduce the need to repeat dose of medication. But, the effectiveness of both drugs for reducing the agitation is equal, based on Ramsey score.

The previous studies showed that using ketamine even with lower doses leads to induced sedation and acceptable analgesic effects. For example, Majidinejad and colleagues displayed that lower dose of ketamine administration has similar effect to morphine in reducing the pain from broken bone (15). Qureshi et al. showed in their study on 30 patients that taking ketamine orally causes the lidocaine injection and suture handling to be well-tolerated for the child (10). To comparison ketamine with nitrous oxide, Lee and colleagues declared that nitrous oxide is a safer drug than ketamine injection, makes faster recovery, and does not induce unnecessarily deep sedation (7). In another research by Jung et al. it was displayed that emergence agitation in pediatric patients need orthopedic surgery does not appear any difference between two groups of ketamine and sodium

Table 1: Demographic and clinical variables in the studied patients

Variable	Therapeutic groups		P[1]
	Ketamine	Thiopental	
Age (month)	30.10±16.88	42.8±18.82	0.013
Gender (%)			
Male	19 (63.33)	20 (66.67)	0.79[2]
Female	11 (36.67)	10 (33.33)	
Vital signs (before intervention)			
Respiratory rate (per minute)	19.27±5.36	15.33±1.26	<0.001
Heart rate (per minute)	106.87±15.64	96.47±4.11	<0.001
Arterial oxygen saturation (%)	96.0±2.72	93.4±1.28	<0.001

[1]Based on Mann-Whitney test

[2] Based on Chi-squared test

Table 2: The efficiency of ketamine and sodium thiopental in induction of sedation

Variable	Therapeutic groups		P
	Ketamine	Thiopental	
Sedition times			
Onset to action (minutes)	7.77±4.13	28.23±5.18	<0.001[a]
Sedation Recovery time (minutes)	29.83±7.70	12.57±2.57	<0.001[a]
Ramsey score	3.70±0.60	3.70±0.60	0.87[a]
Vital signs			
Respiratory rate (per minute)	21.31±5.52	18.13±2.0	0.96[b]
Heart rate (per minute)	115.44±11.93	105.12±3.80	0.33[c]
Arterial oxygen saturation (%)	95.92±3.0	92.12±1.74	0.013[d]

[a] Based on Mann-Whitney test

[b] Based on non-parametric analysis of covariance test; Adjusted for respiratory rate before intervention and age of the patient

[c] Based on non-parametric analysis of covariance test; Adjusted for heart rate before intervention and age of the patient

[d] Based on non-parametric analysis of covariance test; Adjusted for arterial oxygen saturation level before intervention and age of the patient

thiopental (16). In addition, Kim and others stated that intravenous injection and thiopental administration in preoperative holding area have the equal effectiveness in reducing the agitation of separation form parents and have no effect on emergence agitation. This study declared that using sodium thiopental could be a better choice for preanesthetic medication, if monitoring was accurately performed (17). In congruent, the present study shows that effectiveness of these two drugs is the same in reducing agitation of the child. In several other studies it was established that ketamine is more appropriate drug than sodium thiopental. For instance, Yoosefi et al. presented that ketamine administration during electroconvulsive therapy is well-tolerated and leads to faster improving of depression signs, reduce the seizure following the therapy, and better cognitive function in comparison with sodium thiopental (18). Furthermore, Saadawy and others showed that for prevention from the pain of propofol administration, using ketamine is better than sodium thiopental (19). The findings of this study also displayed that using ketamine is the better choice for induction of sedation before suture handling in pediatric patients.

One of the limitations of the present research was the few number of sample size in the studied groups, but it seems that this limitation has no effect on findings. It was determined that the least power of this project in assessing effectiveness and efficiency of ketamine and sodium thiopental was 87%. Because the power of study was in appropriate, the low sample size has no effect on the findings of study.

Conclusion:

The findings of the present study show that the time to onset of action of sodium thiopental is significantly higher than hydrochloride ketamine, while its sedation recovery time is shorter. It is worth noting that the average of arterial oxygen saturation level in ketamine group was more than sodium thiopental (about 4%). As the result, although recovery time from ketamine sedation is more than sodium thiopental, it is considered as the better choice for induction of sedation in pediatric patients need laceration repair. In addition, long-term effect of ketamine provides more time for the physician to do the procedure and may reduce the need to repeat dose of medication. But, the effectiveness of both drugs for reducing the agitation is equal, based on Ramsey score.

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Conflict of interest:

None

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