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ORIGINAL RESEARCH

Oral Chloral Hydrate Compare with Rectal Thiopental in Pediatric Procedural Sedation and Analgesia; a Randomized Clinical Trial

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Abstract

Introduction: The increasing use of diagnostic imaging in pediatric medicine has resulted in growing need for procedural sedation and analgesia (PSA) to minimize motion artifacts during procedures. The drug of choice in pediatric PSA was not introduced until now. The aim of the present study was comparison of oral chloral hydrate (OCH) and rectal sodium thiopental (RST) in pediatric PSA.

Methods: In the present randomized clinical trial, 2-6 years old pediatrics who referred for performing brain computed tomography scan was enrolled and were randomly divided in to two groups. OCH (50mg/kg) and RST (25mg/kg) were prescribed and a trained nurse recorded the time from drug prescription to receiving the conscious sedation (onset of action), the total period which the patient has the Ramsay score≥4 (duration of action), and adverse effect of agents. Mann-Whitney U test and chi-squared test, and Non-parametric analysis of covariance (ANCOVA) were used for comparisons. **Results:** One hundred and forty children were entered to two groups of OCH and RST, randomly. The patients of two groups had similar age, sex, weight, and baseline vital signs except for diastolic blood pressure ($p<0.001$). The onset of action in OCH and RST groups were 24.5±6.1and 28.7±5.2 minutes, respectively ($p<0.001$). Duration of action in OCH and RST groups were 12.9±2.8 minutes and 13.7±2.6 minutes, respectively ($p=0.085$). Non-parametric ANCOVA revealed that only diastolic blood pressure was affected by drug prescription ($p=0.001$). In 11(15.7%) patients in RST group, diarrhea was observed during 24 hours ($p=0.001$). Oxygen desaturation was observed only in two patients, both in OCH group. **Conclusion:** Each of the sedative has advantages and disadvantages that should be considered when selecting one for inducing short-term sedation. It seems that rectal sodium thiopental and oral chloral hydrate are equally effective in pediatric PSA and based on patient's condition we can administrate one of these agents.

Key words: Pediatrics; conscious sedation; anesthesia and analgesia; chloral hydrate; thiopental

Cite this article as: Azizkhani R, Kanani S, Sharifi A, Golshahi K, Masoumi B, Ahmadi O. Oral chloral hydrate compare with rectal thiopental in pediatric procedural sedation and analgesia; a randomized clinical trial. Emergency. 2014;2(2):85-9.

Introduction:

The increasing use of diagnostic imaging in pediatric medicine has resulted in growing need for procedural sedation and analgesia (PSA) to minimize motion artifacts during procedures. The drug of choice in pediatric PSA was not introduced until now. The prescription of most sedative drugs like pentobarbital requires intravenous (IV) route of administration, undesirable for the child and parents (1). Oral chloral hydrate (OCH) is one of the sedative agents, which it is independency from venipuncture turns it to be a considerable alternative for pediatric PSA (2-6). This drug are widely used in pediatric sedation. OCH is used for sedation of children under 6 years old. It is a non-opiate, non-benzodiazepines, and oral hypnotic drug. Most studies showed that it can be considered as a safe and more effective drug for short-term sedation (7-10) with successful rates of 85%–98% (2, 11). But, it has unpleasant taste and some studies showed that it could be carcinogen (12). Another alternative drug is rectal sodium thiopental (RST). For the first time in 1979, rectal route of administration was used for PSA during computed tomography (CT) scan and favorable results achieved. Several studies revealed that rectal sodium thiopental (RST) has an effective role in children's sedation. This drug well absorbed from distal rectum and its effect appears within 5-10 minutes (1, 13-16). Akhlaghpour and his colleagues showed 98% successful rate of RST in pediatric PSA (17). If the children don't suffer from porphyria, diarrhea, breathing problems, active infection, severe cardiovascular disease, and asthma the drug with dose of 25mg/kg is prescribed rectally

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Received: 1 April 2014; Accepted: 5 April 2014

through Nelaton catheter (18).There are a few study regarding the comparison of advantages and disadvantages of above mentioned drugs in pediatric PSA. The aim of the present study was comparison of OCH and RST in pediatric PSA.

Methods:

Study design and setting:

The present randomized clinical trial was prepared based on Helsinki declaration and approved by ethics committee of Isfahan University of Medical Sciences. In addition, the study was registered in Iranian registry of clinical trial. After explanation of sedation protocol, the consent form was obtained from the parents.

Participants

In this project, study population were 2-6 years old pediatrics who referred for performing brain computed tomography scan to Alzahra and Kashani Esfehani Hospitals, Esfehan, Iran, during 2012. They were randomly divided in to two groups of OCH and RST, based on block randomization method. The children with following criteria were excluded from the study: intracranial hypertension, seizure, airway problems like hypertrophie adenoid, ileus or suspected of having intestinal obstruction, liver and kidney disease, sensitivity to barbiturates, porphyria, diarrhea, active infection, cardiovascular disease, asthma, and drug sensitivity.

Intervention

At first, patient's information was collected and recorded to the computerized database by a radiology nursing staff. The database contains information about demographic, clinical and sedation data such as total time of sedation, onset of action, duration of action, and complications**.** They were randomly divided in to two groups of OCH and RST using randomized permuted block design. In OCH group, 50mg/kg of chloral hydrate was drawn in a syringe and administered orally. The consumption box of chloral hydrate was purchased from Merck KGaA Company, Germany. Following drug prescription the sedation score of the patient was evaluated and if it was equal to Ramsay score of four, the child underwent CT scan along with an equipped resuscitation team and continuous pulse oximetry. After 15 minutes if the level of sedation decreased to score<4, another 50mg/kg dose of the drug was prescribed. In the case of decreased oxygen saturation, 100% oxygen delivered using nasal cannula or oxygen mask. In RST group, like the previous group, 25mg/kg of sodium thiopental, diluted to total volume of 10 milliliter with distilled water, was injected through Nelaton catheter, entered five centimeter to the rectum. In this project, the dose of 25mg/kg was used, which is the least effective dose in most of studies (9, 17). If the patient achieved Ramsey score of four, underwent CT scan with similar condition of previous group. If there was, no sedation observed after 15 minutes, 15mg/kg of thiopental sodium like the first time was delivered rectally. The consumed vial was provided from Rote media company, Germany. In both groups, all of the patients underwent continuous pulse oximetry and close monitoring by an emergency medicine resident during and after the time of procedure until full awakening.

Outcome:

Outcome parameters recorded by the nursing included the time from drug prescription to receiving the conscious sedation (onset of action), and the total period which the patient has the Ramsay score≥4 (duration of action). The adverse recorded events included failed sedation, oxygen desaturation (≥ 4% decrease in oxygen saturation), increasing the frequency of defecation during the first 24 hours of drug administration, based on parent's report (diarrhea), and delayed events such as vomiting, hyperactivity, irritability, or other symptoms that caused parental concerns. After full awaking and before discharging the children, warning signs of possible side effects was trained to the parents and contacted them after 24 hours to find and register the side effects concluded breathing problems, diarrhea, and increasing the child activity.

Definitions:

Conscious sedation: In terms of Ramsay sedation scale (19) is the condition that the patient is asleep and response to stimulations slowly (score four).

Hypotension in 1-10 years old children: systolic blood pressure <70 mmHg + (2×age in years)

Statistical analysis

Statistical analysis was performed using a statistical software package (SPSS version 20; Chicago, IL). Mann-Whitney U test and chi-squared test were performed for quantitative and qualitative variables, respectively. In addition, non-parametric analysis of covariance was used for comparison of post procedure's vital signs including respiratory rate (RR); oxygen saturation (O2sat); systolic blood pressure (SBP); and diastolic blood pressure (DBP) between OCH and RST groups. P <0.05 was taken to indicate statistical significance.

Results:

One hundred and forty children were entered to two groups of OCH and RST, randomly. The patients of two groups had similar age, sex, weight, and baseline vital signs except for diastolic blood pressure (p<0.001) (Table1). In OCH and RST groups, 58 (82.9%) and 61 (51.26) patients reached Ramsay score of four, respectively (p=0.49). Rescue doses are administered for 12(17.1%) patients in OCH group and 9 (12.9%) in RST group. Finally, all these patients reached to Ramsay score of four. The onset of action in OCH and RST groups were 24.5±6.1and 28.7±5.2 minutes, respectively (p<0.001). Duration of action in OCH and RST groups were 12.9±2.8 minutes and 13.7±2.6 minutes, respectively (p=0.085) (Figure 1). Table 2 shows the compari-

son of vital signs after the sedation in two groups. Non-parametric ANCOVA revealed that only diastolic blood pressure was affected by drug prescription (p=0.001). Mean diastolic blood pressure after administration of OCH and RST was 60.4±6.95 and 53.9±6.9, respectively. In 11(15.7%) patients in RST group, diarrhea was observed during 24 hours (p=0.001). Oxygen desaturation was observed only in two patients, both in OCH group. Any other side effects were not seen during and after 24 hours of the sedation in two groups.

Discussion:

The increasing use of computed tomography, magnetic resonance imaging (MRI), and interventional radiology has resulted in a growing number of infants who require sedation while undergoing imaging procedures. In this study the clinical safety, effectiveness, and potential side effects of OCH and RST in pediatric PSA were compared. This project found no significant difference between the safeties of the two agents. Adverse events occurred infrequently in both groups. Most of patients were sedated with the first dose of sedative agents and only 21 patients included 17.1% in OCH and 12.9% in RST groups needed rescue dose. In the present trial onset of action was significantly longer in RST compared with OCH group, 28.7±5.2 versus 24.5±6.1 minutes, respectively. There was not seen any significant difference regarding duration of action between two groups. No sedation failure has been seen among them. Most side effects related to diarrhea, were generally minimal and easily treated.

Glasier et al. stated that RTS is a safe and effective agent for sedation of infants and children with a 96% successful rate (1). Efficacy and safety of OCH and RST were compared in some studies. In a recent study Granados et al. demonstrated a 97% successful rate of RST in pediatric PSA and declared diarrhea (12.6%) as the most prevalent side effect (20). The mean duration of action for RST was 8.04 minutes in Akhlaghpoor et al. study, which is five minutes less than our result (17). For decades, OCH has been widely used for short-term sedation of children (11, 21, 22). The acute toxicity of OCH is low in recommended single doses. However, acute overdoses may cause cardiorespiratory depression (23, 24). In the present study, we observed 2.9% of OCH treated patient suffered from desaturation, which is slightly higher than other studies. In a most recent study, Finnemore et al. revealed that using OCH let to desaturation in 0.7% of neonates undergo MRI (25). Litman et al. showed 2.2 % preterm and term infants afflicted desaturation following OCH administration (26). Overall, desaturation was the most side effect of OCH like the present study. In co mparison between OCH and RST, because of serious side effect of OCH, it seems that RST is better than OCH. Although, 15.7% of RST cases suffered

Table 1: Baseline characteristics of the study groups

Characteristics	Chloral hydrate	Sodium thiopental	P*
Age (year)	3.8±1.6	3.5±1.5	0.31
Gender (%)			
Male	45 (51.1)	43 (48.9)	0.73
Female	25(48.1)	27(51.9)	
Weight (Kg)	14.54±4.33	15.80±4.44	0.11
RR (per minute)	16.4±2.1	15.9±1.4	0.30
O_2 sat (%)	93.9±1.0	93.5±1.3	0.09
PR (per minute)	96.6±5.4	98.3±4.9	0.14
SBP (mmHg)	101.7±7.3	103.4±7.7	0.07
DBP (mmHg)	61.7±6.7	56.5±7.0	<0.001

*All p values derived from Mann-Whitney U test except gender (Chi-squared test). RR: respiratory rate; O2 sat: oxygen saturation; PR: pulse rate; SBP: systolic blood pressure; DBP: diastolic blood pressure

Table 2: Vital signs before and after sedation in the study groups

Parameters	Chloral hydrate	Sodium thiopental	P*
RR (per minute)	20.3±1.8	19.7±2.3	0.25
O_2 sat (%)	91.6±1.1	91.2±1.4	0.17
PR (per minute)	109.8±6.95	108.4±7.5	0.12
SBP (mmHg)	101.4±7.3	103.9±7.7	0.16
DBP (mmHg)	60.4±6.95	53.9±6.9	0.001

*All p values derived from Non-parametric ANCOVA adjusted for pre-treatment level of variable except pulse rate (Mann-Whitney U test). RR: respiratory rate; O_2sat: oxygen saturation; PR: pulse rate; SBP: systolic blood pressure; DBP: diastolic blood pressure

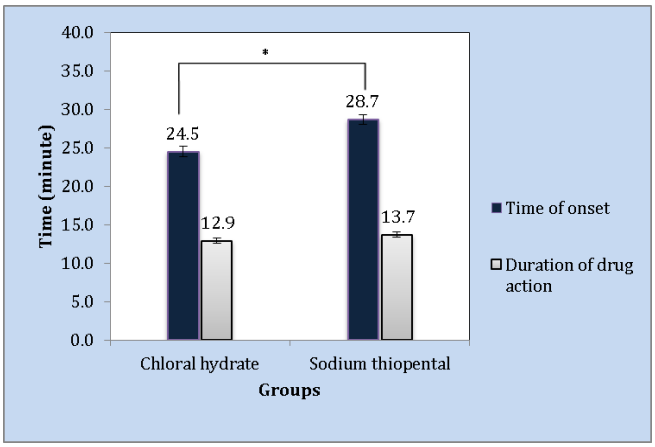

Figure 1: Time of onset and duration of action (Ramsay score of four). * p<0.001.

from mild diarrhea and only 2.9 OCH treated patients experienced the oxygen desaturation, the OCH side effect may be hazardous. In addition, the mild rectal irritation and diarrhea related apparently to rectal administration, generally acceptable for parents and physicians. It was consistent with Rooks et al. study, implied the better safety and effectiveness of pentobarbital (is a short-acting barbiturate like RST) than OCH (27). However, RST has some limitation for instance; it should be avoided in patients with known or suspected rectal trauma or severe thrombocytopenia. Infants younger than three months were not sedated with rectal thiopental because they tend to expel the drug from the rectum. In total RST is more favorable than OCT in our study due to the ease of administration, rapid onset of action, safety, and better compliance.

Limitations:

The limitations of this study were its small sample size and short duration of follow up. Therefore, it is suggested that further studies be conducted with larger sample size, longer follow up periods and different dosages of OCT and RST.

Conclusion:

Each of the sedative has advantages and disadvantages that should be considered when selecting one for inducing short-term sedation. It seems that rectal sodium thiopental and oral chloral hydrate are equally effective in pediatric PSA and based on patient's condition we can administrate one of these agents.

Acknowledgments:

The authors appreciate the insightful cooperation of staffs of the Emergency Department of Alzahra and Kashani Esfehani Hospitals in isfahan, Iran.

Conflict of interest:

None

Funding support:

None

Authors' contributions:

All authors passed four criteria for authorship contribution based on recommendations of the International Committee of Medical Journal Editors.

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