Original Article

CMJ

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Effects of Dextrose Supplementation on Chloral Hydrate Sedation: A Double-Blinded, Randomized, Prospective Study

Young Kwon Koh[1], Han Gil Kang[2], and Young Kuk Cho[1,*]

[1]Department of Pediatrics, Chosun University Hospital, College of Medicine Chosun University, [2]Chonnam National University Medical School, Gwangju, Korea

Sedation plays a crucial role in successful pediatric imaging, and chloral hydrate is commonly used for this purpose. However, the challenges associated with chloral hydrate administration, such as its unpleasant taste and potential induction of vomiting, remain a concern. Sweet oral solutions have emerged as potential solutions for reducing distress and providing analgesia. This study compared the efficacy of dextrose combined with chloral hydrate with that of conventional sedation methods. This prospective, double-blind, randomized controlled clinical study enrolled 160 pediatric outpatients scheduled for echocardiography. Chloral hydrate syrup (100 mg/mL) was supplemented with a dextrose solution (dextrose group) or distilled water (control group) in a 1:10 volume ratio. The sedation achievement time, Skeie scale score, revised Face, Legs, Activity, Cry, and Consolability (FLACC) score, and side effects (nausea, vomiting, hypoxia, and respiratory depression) were assessed. No significant difference in average time to achieve sedation was observed between the dextrose and control groups (24.4±17.8 vs. 24.7±17.1 min, p=0.92). Both groups demonstrated similar levels of sedation according to the Skeie scale and mean revised FLACC score. Although the occurrence rates of nausea and vomiting had no significant differences, the dextrose group had no cases of vomiting in children aged >24 months compared to the control group, which had three cases (30%). In conclusion, the addition of dextrose to chloral hydrate did not significantly affect sedation time, anxiety, pain reduction, or occurrence of gastrointestinal complications during sedation.

Key Words: *Dextrose; Sedation; Chloral Hydrate*

Article History:
Received July 21, 2023
Revised August 10, 2023
Accepted August 29, 2023

Corresponding Author:
Young Kuk Cho
Department of Pediatrics,
Chosun University Hospital,
365 Pilmun-daero, Dong-gu,
Gwangju 61453, Korea
Tel: +82-62-220-3040
Fax: +82-62-227-2904
E-mail: youngcx@chosun.ac.kr

INTRODUCTION

In pediatric cases, successful imaging often requires sedation, and chloral hydrate is commonly used for this purpose.[1] Although there are alternative options for safe and effective sedation in children undergoing imaging studies, chloral hydrate is considered superior in terms of safety and efficacy owing to its higher lethal-to-therapeutic dose ratio compared with those of barbiturates. Additionally, chloral hydrate has been associated with fewer instances of respiratory depression relative to other sedation drugs.[2] However, complications such as hypoxia, respiratory depression, hyperactivity, nausea, vomiting, and inadequate sedation are frequently reported with its use.[3] Of these complications, the main challenge of using chloral hydrate is its unpleasant taste and tendency to induce vomiting, making accurate dosing difficult, particularly in infants.[3]

Several studies have reported that an oral dextrose solution reduces behavioral distress during minor procedures and possesses analgesic effects.[4-8] For instance, Gharehbaghi and Ali[4] demonstrated that dextrose had a statistically significant antinociceptive effect compared to sterile water, reducing the immediate behavioral pain response and shortened crying time after venipuncture. Similarly Akman et al.[6] observed that dextrose solutions decreased crying time and pain scores during the heel prick in newborn infants.

https://doi.org/10.4068/cmj.2023.59.3.174

Therefore, we investigated the potential of dextrose-combined chloral hydrate as a means to ameliorate these complications. This study aimed to assess whether the addition of dextrose to chloral hydrate would result in successful sedation in children and to address the primary difficulty associated with conventional chloral hydrate administration.

MATERIALS AND METHODS

1. Patient selection and study design

In total, 160 children, including infants with known or suspected heart disease, were enrolled in this study. This prospective randomized controlled clinical trial was conducted at the outpatient pediatric cardiology clinic of Chonnam National University Hospital between April 2010 and December 2011. Medical histories and physical examinations of all children were conducted by both nurses and pediatricians. Data on height, weight, heart rate, respiratory rate, and oxygen saturation were collected from each patient. Informed parental consent was obtained from legal representatives before participation. The exclusion criteria included patients with hemodynamically significant heart diseases, such as those on heart failure medication, as well as individuals with cardiomyopathy, acute myocarditis, neurologic impairment, and respiratory compromise that could potentially affect sedation. In this double-blind study, patients received either chloral hydrate with dextrose or chloral hydrate with distilled water orally before echocardiography. Randomization and administration of the solution were carried out by a nurse who was not involved in the study's measurements.[4] Of the total participants, 78 patients received chloral hydrate combined with dextrose (dextrose group, mean age: 14.9±10.3 mo., body weight: 9.9±2.3 kg), while 82 patients received chloral hydrate combined with distilled water (control group, mean age: 15.2±7.0 mo., body weight: 10.2±1.9 kg). A 10% dextrose solution or distilled water was added to the chloral hydrate syrup at a density of 100 mg/mL in a 1:10 volume ratio to create experimental and control solutions. The prepared chloral hydrate syrup was administered at doses of 50-75 mg/kg, with a maximum dose of 2,000 mg.[9] Additional doses of the prepared solution were administered at 30-minute intervals after the first dose if the patients were not adequately sedated. Oral medications were administered directly into the oral cavity using a syringe while the parent held the patient.

2. Sedation and pain assessment

All children were monitored in accordance with the revised guidelines of the American Academy of Pediatrics. This monitoring included continuous electrocardiographic monitoring of heart rate, continuous pulse oximetry monitoring of arterial hemoglobin oxygen saturation, intermittent assessment of airway patency, and impedance pneumography monitoring of respiratory rate.[9]

All children followed appropriate dietary restrictions before sedation. Infants under 5 months of age had solid food restricted for 4 hours, infants between 6 and 36 months had a 6-hour restriction, and infants over 36 months had an 8-hour restriction. Clear liquids were allowed up to 2 hours before sedation.[9] Trained pediatric nurses evaluated the sedation levels and pain scores of the patients. Sedation assessment was performed 20 min after administration of the prepared solution during the echocardiogram and 5 min after the echocardiogram ended, using the Skeie scale, which ranges from 0 to 4 as follows: (0) patient awake and tense, (1) patient awake but not tense, (2) patient drowsy, (3) patient sleepy but arousable, and (4) patient sleepy and not arousable.[10]

Pain assessment using the revised Face, Legs, Activity, Cry, and Consolability (FLACC) scale was evaluated by pediatric nurses before, during, and 20 min after the administration of the prepared solution. The revised FLACC scale comprises five categories, each scored from 0 to 2, providing a total score ranging from 0 to 10.[8] The pain score is directly proportional to the degree of perceived pain.[11]

Data regarding the total dose of medication administered, time required to achieve sufficient sedation for performing echocardiography, and adverse events, including sedation failure, nausea, and vomiting, were collected and documented by the medical staff.

The time taken to achieve the appropriate sedation level was measured from the initial intake of the solution to a sedated state in which the patient was not easily aroused by minor stimulation. Inappropriate sedation within 2 h of the maximum dose was defined as sedation failure.[12]

3. Statistical analysis

Descriptive statistics are presented as means±standard deviations (SDs), medians with ranges for quantitative variables, and numbers (percentages) for qualitative variables. Mean age, body weight, average time to sedation, Skeie scale, and revised FLACC score are described as means and SDs, and group comparisons were conducted using Student's t-test. A Fisher's exact test was used to compare the proportions between the two groups by sex and to evaluate the differences in the occurrence rates of gastrointestinal adverse events between the experimental and control groups. A univariate analysis was performed using the Student's t-test and Pearson's chi-square test when appropriate. An analysis of variance was conducted to compare data among more than three groups, such as average time to achieve sedation, Skeie scale, and revised FLACC score according to three age categories in dextrose and control groups, followed by Tukey's honest significant difference post hoc test. When homogeneity of variance was not present according to Levene's test, Dunnett's T3 test was used as the post-hoc test. When a normal distribution was not observed, as assessed using the Shapiro–Wilk test, the Kruskal–Wallis test was used, followed by Bonferroni correction. Significance was set at $p < 0.05$. All analyses were performed using SPSS 18.0 for Windows (SPSS, Chicago, IL, USA).

4. Ethics statement

This study was approved by the Institutional Review Board of the Chonnam National University Hospital (protocol no. I-2009-07-076). All data collected in this study remained confidential.

RESULTS

Altogether, 160 patients received either chloral hydrate combined with dextrose (n=78, dextrose group) or chloral hydrate combined with distilled water (n=82, control group). The patients were subdivided into three groups according to age (<12, 12-24, and >24 months).

No significant differences in sex or body weight were observed among the different age groups in either the dextrose and control groups (Table 1). The median dose of chloral hydrate was 77 mg/kg (range, 45-118 mg/kg) in the dextrose group and 79 mg/kg (range, 43-120 mg/kg) in the control group. Sedation was successful in 74 (94.9%) of the 78 dextrose group examinations and in 77 (93.9%) of the 82 control group examinations.

In the dextrose group, failure to achieve sedation occurred in 0 (0.0%) children aged <12 months, 3 (10.3%) children aged between 12 and 24 months, and 1 (10.0%) child aged >24 months. In the control group, failure to achieve sedation occurred in 3 (9.1%) children aged <12 months, in 1 (2.6%) child aged between 12 and 24 months, and in 1 (10.0%) child aged >24 months.

Table 2 presents the average time to achieve sedation among the different age groups in the dextrose and control groups. No significant difference regarding the average time to achieve sedation in all ages was observed between the dextrose and control groups (24.4±17.8 and 24.7±17.1 min, respectively, p=0.92). There was also no significant difference between the dextrose and control groups regarding the average time to achieve sedation according to age (Table 2).

The level of sedation according to the Skeie scale among different age groups in both the dextrose and control groups demonstrated no significant difference at all three measure points as follows: 20 min after administration of the prepared solution (3.7±1.5 and 3.6±1.3, respectively, p=0.75), during examination (4.5±0.9 and 4.5±0.8, respectively, p=0.95), and 5 min after examination (4.4±0.9 and 4.5±0.8, respectively, p=0.64) (Table 3).

The mean revised FLACC scores of the dextrose and control groups before and during the administration of the chloral hydrate solution are presented in Table 4. The revised FLACC scores before the administration of chloral hydrate solution were significantly higher in the dextrose group than the control group (0.7±2.1 and 0.0±0.0, respectively, p<0.01). No significant differences during the administration of chloral hydrate solution were observed between the dextrose group and control group (5.6±2.5 and 6.0±2.4, respectively, p=0.29).

Fig. 1 illustrates the number of patients with nausea and vomiting in the dextrose and control groups. For children aged <12 months in the dextrose group, nausea occurred

TABLE 1. Characteristics of chloral hydrate sedation with dextrose (dextrose group) or with distilled water (control group) according to age

	Dextrose group	Control group	p-value
<12 mo	n=39	n=33	
Age (mo)	8.9±1.7	8.6±1.5	0.43
Body weight (kg)	8.5±1.2	8.7±1.3	0.60
Sex (boy/girl)	16/23	14/19	1.00
12-24 mo	n=29	n=39	
Age (mo)	16.6±4.1	17.2±3.3	0.54
Body weight (kg)	10.4±1.4	10.8±1.3	0.35
Sex (boy/girl)	17/12	18/21	0.34
≥24 mo	n=10	n=10	
Age (mo)	33.3±7.5	28.7±3.3	0.42
Body weight (kg)	13.8±2.6	13.1±1.1	0.45
Sex (boy/girl)	7/3	10/0	0.21
Total	n=78	n=82	
Age (mo)	14.9±10.3	15.2±7.0	0.87
Body weight (kg)	9.9±2.3	10.2±1.9	0.38
Sex (boy/girl)	40/38	42/40	1.00

TABLE 2. Average time to achieve sedation in the dextrose and control groups according to age

	Dextrose group (min)	Control group (min)	p-value
<12 mo	19.5±12.4	21.0±14.3	0.65
12-24 mo	30.6±20.0	28.8±19.0	0.72
≥24 mo	27.8±25.6	19.4±13.8	0.40
Total	24.4±17.8	24.7±17.1	0.92

TABLE 3. Skeie scale at 20 min after chloral hydrate administration (before examination), during examination (during exam), and at 5 min after the end of the examination (after exam) in the dextrose and control groups according to age

	Dextrose group			Control group		
	Before exam	During exam	After exam	Before exam	During exam	After exam
<12 mo	4.0±1.3	4.6±0.6	4.5±0.8	4.0±1.1	4.5±0.6	4.5±0.5
12-24 mo	3.3±1.5	4.2±1.2	4.4±1.0	3.4±1.4	4.5±0.7	4.5±0.7
≥24 mo	3.2±1.9	4.6±0.5	4.6±0.5	3.1±1.5	4.4±1.7	4.4±1.7
Total	3.7±1.5	4.5±0.9	4.4±0.9	3.6±1.3	4.5±0.8	4.5±0.8

TABLE 4. Revised-Face, Legs, Activity, Cry, and Consolability (FLACC) scale before and during administration of chloral hydrate in the dextrose and control groups according to age

	Dextrose		Control	
	Before administration	During administration	Before administration	During administration
<12 mo	0.6±1.9	5.8±2.2	0.0±0.0	6.5±2.4
12-24 mo	0.6±1.9	5.8±3.1	0.0±0.0	6.0±2.1
≥24 mo	1.5±3.5	3.8±3.1	0.0±0.0	4.2±2.9
Total	0.7±2.1	5.6±2.5	0.0±0.0	6.0±2.4

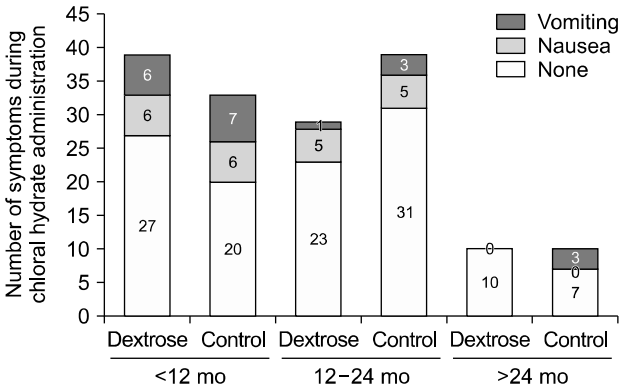

FIG. 1. Number of cases of nausea and vomiting during administration of chloral hydrate in the dextrose and control groups according to age.

in 6 (15.3%) patients, and vomiting occurred in 6 (15.3%) patients. In the control group, nausea and vomiting occurred in six (18.2%) and seven (21.2%) patients, respectively. No significant difference in the occurrence rates of nausea and vomiting was observed between the two groups (p=0.75 and p=0.55, respectively). For children aged between 12 and 24 months in the dextrose group, nausea occurred in five (17.2%) patients, and vomiting occurred in one (3.4%) patient. In the control group, nausea and vomiting occurred in five (12.8%) and three (7.7%) patients, respectively. No significant difference in the occurrence rates of nausea and vomiting was observed between the two groups (p=0.74 and p=0.63, respectively). Meanwhile, nausea and vomiting were not observed in children aged >24 months in the dextrose group. In the control group, nausea did not occur, and vomiting occurred in three patients (30.0%). No significant difference in the rate of vomiting was observed between the two groups (p=0.21).

Repeated chloral hydrate administration was carried out in 15 children within the dextrose group and another 15 children within the control group. Among the control group, eight cases (11.9%) experienced vomiting with a single chloral hydrate sedation, while five patients (33.3%) encountered vomiting in the repeated dosing group. No significant distinction in the incidence rates of vomiting was observed between the single and repeated chloral hydrate administrations (p=0.06). In the dextrose group, four instances (6.3%) of vomiting occurred with a single chloral hydrate sedation, while five cases (20.0%) were observed in the repeated dosing group. A significant difference in the occurrence rates of vomiting was not noted between the single and repeated chloral hydrate administrations groups (p=0.12).

No episodes of cardiovascular complications were detected, and none of the patients required hospitalization for complications associated with dextrose and distilled water-combined chloral hydrate sedation.

DISCUSSION

In this study, the addition of a dextrose solution to chloral hydrate did not result in significant changes in the average time to achieve sedation, Skeie scale scores, revised FLACC scores, or the occurrence of gastroenteritis complications such as nausea and vomiting, when compared with the control group receiving distilled water.

The main challenge associated with using chloral hydrate is its unpleasant taste, which can lead to infants resisting swallowing or experiencing vomiting, making accurate dosing difficult.[3,13] A previous study has highlighted the effectiveness and safety of pentobarbital compared to chloral hydrate, with the taste of the phenobarbital solution identified as a factor that improves compliance.[14] To address this challenge, the use of dextrose solution as an adjunct to alleviate the unpleasant taste of chloral hydrate has been proposed, and its analgesic and sedative effects have been observed in studies involving newborns and animals.[9,15] Multiple studies investigating different types of sugar support the hypothesis that the analgesic effect of oral sweet solutions is based on the perception of sweetness.[16,17] The underlying mechanism may involve the release of endogenous opiates triggered by the perception of a sweet taste.[18] In our study, we employed a dextrose mixture with chloral hydrate to reduce the incidence of vomiting. Although we did not observe a statistically significant effect of dextrose supplementation on chloral hydrate sedation, no cases of vomiting were recorded in the dextrose group among children aged >24 months compared to three cases (30.0%) in the control group. It's worth noting that this finding may have been influenced by the relatively low enrollment numbers, particularly among children aged over 24 months, with only 10 participants in both the dextrose and control groups. Vade et al.[9] conducted a study to determine the frequency of adverse events associated with chloral hydrate sedation in children under-

going computed tomography and magnetic resonance imaging. They reported that the rate of gastrointestinal adverse events, including vomiting, in chloral hydrate sedation for children under 1 year of age was 4%, which stands in contrast to our study's higher rates in both the dextrose (9.0%) and control (15.9%) groups. Given these variations, comprehensive large-scale prospective investigations are warranted to further explore the impact of dextrose supplementation on chloral hydrate sedation.

In our study, the average time to achieve sedation in both the dextrose and control groups for all age groups was approximately 24.4±17.8 min and 24.7±17.1 min, respectively, with no significant differences observed. Previous reports have indicated a sedation success rate of 72% within 30 min of chloral hydrate administration in children aged <12 months.[9] In our data, for children aged <12 months, the average time to achieve sedation in the dextrose and control groups was 19.5±12.4 min and 21.0±14.3 min, respectively.

Effective pain assessment is crucial for optimal care in children, particularly in cases where self-reporting is not possible owing to cognitive impairment.[19] The r-FLACC scale has demonstrated reasonable interrater reliability and validity as a measure of pain in children with varying degrees of cognitive impairment.[11] In our study, the r-FLACC scale was used to assess pain intensity before, during, and 20 min after the administration of chloral hydrate solution added with dextrose solution or distilled water. Although we did not observe a significant effect of dextrose supplementation on chloral hydrate sedation, the r-FLACC scale proved to be an effective tool for measuring pain intensity in young children undergoing sedation.

This study has certain limitations. Firstly, the small sample size hinders the extrapolation of actual adverse event incidence to a larger population. Secondly, due to the double-blind design, achieving age- and sex-matched distributions in the two groups was unfeasible. Thirdly, we did not assess participants' previous exposure to chloral hydrate for sedation, which could potentially influence sedation failure or achievement time. Fourthly, the duration of sleep differences between the two groups was not investigated. Fifthly, our choice of a 10% dextrose and chloral hydrate ratio at a 1:10 volume ratio may not yield a sufficient therapeutic effect. The quality and intensity of the sweet taste significantly impacted our experiment, prompting the need for further studies exploring different dextrose doses or types of sugars. Hence, further investigation is warranted to address these limitations and enhance our understanding.

In conclusion, the addition of dextrose to chloral hydrate did not have an additive effect on sedation time, anxiety, pain reduction, or the occurrence of gastrointestinal complications during sedation.

ACKNOWLEDGEMENTS

This study was supported by a research fund from the Chosun University (2020).

CONFLICT OF INTEREST STATEMENT

None declared.

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