

# ORIGINAL ARTICLE

## Comparison of Chloral Hydrate Solution, Hydroxyzine Syrup, and Lidocaine/Prilocaine Cream as Premedication for Lumbar Puncture in Children: A Double-Blind Study

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## Abstract

### Objectives

This study aimed to compare the clinical effectiveness of oral hydroxyzine and chloral hydrate to topical lidocaine/prilocaine 2.5% cream as premedication in pediatric leukemia patients.

### Materials & Methods

This double-blind clinical trial study was conducted on 70 leukemic and nonleukemic patients aged 3-11 years. The patients were divided into four groups. In group A, chloral hydrate solution was given to 18 patients. In group B, hydroxyzine syrup was used for 18 patients. In group C, chloral hydrate solution and lidocaine/prilocaine cream were used for 17 patients. In group D, hydroxyzine syrup and lidocaine/prilocaine cream were used for 17 patients. These groups were assessed and judged based on the visual analog scale (VAS). The side effects of the drugs were also recorded.

### Results

In this study, 54.3% (n=38) and 45.7% (n=32) of the cases were female and male, respectively. Furthermore, 77%, 7.2%, and 15.8% of the cases were reported with acute lymphocytic leukemia, acute myeloid leukemia, and infectious disease, respectively. The VAS results showed no difference in these four groups. Nontraumatic lumbar puncture (LP) (red blood cell < 50) was observed in 97.1% of the cases.

### Conclusion

Although premedications for LP with hydroxyzine syrup and chloral hydrate solution were not statistically effective in pain relief, they

increased patient and parent satisfaction. Moreover, adding lidocaine/prilocaine cream does not improve the effectiveness of the drugs.

**Keywords:** Lumbar Puncture; Premedication; Chloral Hydrate; Hydroxyzine; Lidocaine/Prilocaine Cream

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## Introduction

Although lumbar puncture (LP) essentially is a painful and stressful procedure, it is indicated for diagnosis or therapeutic purposes in leukemic and nonleukemic patients (1). The nontraumatic results of this procedure in decreasing central nervous system (CNS) disease and proper diagnosis make LP a cornerstone in treatment protocols (2). According to pain and anxiety related to the procedure, these patients' quality of life might change. Therefore, the American Academy of Pediatrics advises anesthetic and sedative drugs in painful procedures in children (3).

A good premedication should be safe, have low side effects, early initiation of action, and short recovery time, and do not compromise vital organs. Potent sedative agents, such as midazolam (4), propofol (5), and ketamine (6), need cardiac monitoring, blood pressure measuring, pulse-oximetry monitoring, nursing supervision, and maintaining the intravenous route. Older oral sedatives and analgesics and local analgesic agents are more available in many secondary and tertiary centers in developing countries with negligible side effects on cardiovascular systems. Chloral hydrate solution (7), promethazine (8), and nitrous oxide (9) are used more than other agents as premedication in painful procedures in children. Otherwise, topical analgesic agents, such as prilocaine/lidocaine (EMLA) cream (10), were usually recommended before painful procedures

in children previously. This study was designed to compare the efficacy of chloral hydrate solution, hydroxyzine syrup, and prilocaine/lidocaine cream as premedication in LP in pediatric patients.

## Materials & Methods

The study was a double-blind clinical trial conducted on 70 cases (55 oncology outpatients, 5 oncology inpatients, and 10 infectious inpatients). The patients were within the age range of 3-11 years of both genders scheduled to undergo LP due to leukemic CNS prophylaxis or diagnosis of meningitis. The patients were allocated randomly into four groups. The patients in group A were premeditated with chloral hydrate solution (50 mg/kg, maximum dose of 1000 mg) and the placebo ointment (vitamin A). In group B, premedication was given with hydroxyzine syrup (0.6 mg/kg) and the placebo ointment (vitamin A). Group C was premeditated with chloral hydrate solution (50 mg/kg, maximum dose up to 1000 mg) and prilocaine/lidocaine 2.5% cream. Finally, in group D, in addition to hydroxyzine syrup (0.6 mg/kg), prilocaine/lidocaine 2.5% cream was used as premedication.

Randomization was performed by a computer-generated list of patients in four groups. The prepared list was concealed in opaque sealed envelopes that were numbered and opened sequentially after obtaining consent from parents. Premedication in the form of syrup and topical

ointment/cream was given 15 minutes before the procedure in the presence of their parents. The patients were excluded from the study in the case of allergic reaction to these drugs, any lumbosacral area abnormality or infections, or severe thrombocytopenia (<50000). The patients were monitored by pulse-oximetry, nasal end-tidal capnography, and serial blood pressure measurements before and after the procedure.

Premedication efficacy was assessed by a trained observer using the Observational Scale of Behavioral Distress-Revised. After the procedure, the standard face scale questionnaire, the visual analog scale (VAS), was completed by the examiner, nurse, and parents (or patients). Any side effects of this intervention were asked about and marked on the checklist during the next 24 hours. Less than 50 red blood cells (RBC) per milliliter of cerebrospinal fluid (CSF) was considered nontraumatic (10). Statistical analysis was performed by the student's t-test and Chi-square test at the significance level of 0.05. Then, the data were analyzed using SPSS software (version 22).

## Results

A total of 38 female (54.3%) and 32 male (45.7%) patients were included in this study (Table 1). The

patients' mean age value was 83.9130.185± months. In each of groups A and B, 18 patients, and in each of groups C and D, 17 patients were included. There was no significant difference in patients' age in the four groups (P=0.915). The underlying conditions of patients who entered the study were acute lymphocytic leukemia (77%), acute myeloid leukemia (7.2%), and infectious disease (15.8%) (LP was performed to rule out the possibility of meningitis). The children's pain, evaluated by self-administered VAS, showed overall satisfaction of children and their parents. According to the VAS, the mean values of pain were 2.28, 1.26±2.28, 1.26±1.36±1.88, and 2.00±1.32 in groups A, B, C, and D, respectively, with no significant difference (P=0.78); however, the parents and patients had more satisfaction with chloral hydrate solution and hydroxyzine syrup premedications (Table 2).

After 24 hours of the procedure, no side effects (e.g., hematoma, apnea, vomiting, hypotension, and post-LP headache) were recorded in all four groups. The nontraumatic procedure (RBC<50 in CSF analysis) was followed in 97.1% of the cases. Only 2.9% of the cases had traumatic LP (>50 RBC).

**Table 1.** Basic Characteristics of Patients

	Group A n (%)	Group B n (%)	Group C n (%)	Group D n (%)	Total n (%)
<b>Male</b>	8 (25.00)	10 (31.25)	5 (25.63)	9 (28.13)	32 (100)
<b>Female</b>	10 (26.31)	8 (20.05)	12 (31.57)	8 (20.05)	38 (100)
<b>ALL</b>	13 (24.07)	14 (25.92)	13 (24.07)	14 (25.92)	54 (100)
<b>AML</b>	1 (20.00)	1 (20.00)	2 (40.00)	1 (20.00)	5 (100)
<b>Infection</b>	4 (36.36)	3 (27.27)	2 (18.18)	2 (18.18)	11 (100)

ALL, acute lymphocytic leukemia; AML, acute myeloid leukemia

Table 2. Pain Perception Level in Different Groups

Groups	n (%)	Pain level MeanSD	Minimum level	Maximum level
Group A	18 (26)	2.28	1	5
Group B	18 (26)	2.221.263	1	5
Group C	17 (25)	1.881.364	0	4
Group D	17 (25)	2.001.264	0	5

SD, standard deviation

### Discussion

The LP primarily is a painful and stressful procedure; however, it is essential for diagnosis and therapeutic purposes and inevitable in many cases (7). In addition to pain and anxiety for patients and parents, there is the possibility of psychological side effects, such as learning and memory impairment and mental illnesses in the future (11). Otherwise, some studies reported that decreased usage of sedation leads to a high rate of traumatic or failed sampling (12). Otherwise, although topical premedication decreases the procedure’s pain in some studies, it does not decrease failed sampling on personal experience (13). Some studies showed that only 24-33% of neonates received any type of local anesthesia for LP (14, 15). The oncology unit patients suffer from the side effects of chemotherapy, which might include painful procedures; therefore, it is essential to enhance the quality of life of these patients. The ideal sedative agents for children should be safe and easy to administer, have a rapid and predictable onset of action, constant efficacy, a short duration of action, easy reversibility, and minimal cardiovascular and respiratory effect, and produce amnesia and analgesia.( 15)

One of the oldest methods of local analgesia is the use of topical lidocaine, which is still used

in LP. Some studies suggested that the topical application of low doses of lidocaine might be ineffective; therefore, “needle-free jet injection” is an alternative (16). Recently, some studies have proposed EMLA cream instead, even for skin laceration (17). In the reviewed articles, almost all studies focused on comparing oral premedications, and some studies focused on comparing topical premedications. However, the combination of topical and oral premedications was not studied (14).

Otherwise, repeated attempts and needling to obtain a successful LP will aggravate anxiety. The present study compared the efficacy of chloral hydrate solution, hydroxyzine syrup, and prilocaine/lidocaine cream as premedication in LP pediatric patients. Previously, Derakhshanfar et al. compared chloral hydrate, midazolam, and promethazine as premedication for LP. Based on two articles by Derakhshanfar et al., it seems that chloral hydrate, midazolam, and promethazine have sedative efficacy in LP; nevertheless, their effectiveness is in decreasing order (6, 7).

In addition, prilocaine/lidocaine cream (EMLA) and lidocaine ointment recommended by many studies as premedication for LP (9) have additive effects to propofol (11). It can be emphasized that if the addition of lidocaine to oral premedications,

such as chloral hydrate and hydroxyzine, increases analgesia, it might be helpful to decrease the dosage of oral premedication. In addition, it is not necessary to use potent analgesics, such as ketamine, propofol, and midazolam, which might need nursing supervision and cardiovascular monitoring; therefore, numerous life-threatening side effects can be avoidable.

The present study showed that analgesia with topical prilocaine/lidocaine cream is not effective when added to chloral hydrate solution and hydroxyzine syrup for LP sedation. Nevertheless, parents themselves were more satisfied with chloral hydrate solution and hydroxyzine syrup premedications in this study. These two drugs had the same effect in sedation before the LP procedure. Based on the literature review, the first-generation antihistamine, such as hydroxyzine, has not been effective for LP premedication. In one study, the addition of chloral hydrate to midazolam, compared to promethazine syrup, was more effective for analgesia in dental procedures (12).

## In Conclusion

Although the coadministration of chloral hydrate and hydroxyzine did not statistically have a significant effect on pain relief, parents felt more satisfied with the drug than the placebo. On the other hand, adding prilocaine/lidocaine 2.5% cream to oral chloral hydrate or hydroxyzine did not change pain perception.

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## Author's Contribution

Dr Esfehni conceived and designed the analysis. Dr Sahraii collected the data. Dr Seif Rabie contributed data or analysis tools and performed the analysis. Dr hosseini wrote the paper. Dr Sedigi and Dr Esfehni performed revision of the paper

## Conflict of Interest

None

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