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Effect of Oral Dimenhydrinate in Children with Acute Gastroenteritis: A Clinical Trial

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ABSTRACT

Objectives: One of the major causes of mortality in children is acute gastroenteritis. Vomiting is common in early stages of the disease. The aim of this study was to determine the effect of oral dimenhydrinate (DH) in the control of vomiting in cases of acute gastroenteritis in children. ***Methods***: This double-blind, randomized, clinical trial was conducted in a university-affiliated hospital in a western province of Iran. Two hundred children aged one to 12 years old were randomly assigned to either drug or placebo groups. Children in the drug group received oral DH as four doses of 1 mg/kg every six hours (maximum 200 mg), and children in the placebo group received a placebo drug. The patients variables were compared 24 hours after receiving the first dose and at seven and 14 days after discharge. ***Results:*** The mean number of episodes of vomiting was 4.4±2.5 in the drug group versus 4.4±2.1 in the placebo group, which was not statistically significant (p<0.050). The mean number of episodes of diarrhea was 7.4±3.2 and 10.1±2.8 in the drug and placebo groups, respectively, (p<0.050). The duration of diarrhea, side effects, need to revisit, and parent's satisfaction in both groups were also significantly different (p>0.050). ***Conclusions:*** Oral DH in children with acute gastroenteritis does not reduce the number and duration of vomiting. However, our results showed that consumption of DH in acute gastroenteritis patients was effective in reducing the frequency and duration of diarrhea and further investigation into this is warranted.

Acute gastroenteritis can lead to severe morbidity in affected children. Annually, gastroenteritis accounts for millions of deaths in children aged under four years old in Asian, Latin American, and African countries. It is estimated that 450 million cases of diarrhea in children under five years old occur every year and that 1–4% of cases results in death.[1,2]

Infections of the gastrointestinal tract caused by bacterial, viral, or parasitic pathogens are called gastroenteritis. The most common manifestations are diarrhea and vomiting.[3] Most children have vomiting in first stages of acute gastroenteritis; this limits oral rehydration therapy.[4–6]

The benefits of antiemetic and anti-nausea drug use in children with acute gastroenteritis is controversial. However, studies show that physicians often prescribe these drugs. For example, the effectiveness of ondansetron in decreasing nausea in children with acute gastroenteritis has been shown in many studies.[7–14]

Dimenhydrinate (DH) is often used as a medication for nausea, emesis, and vertigo. In Canada, it is used to control vomiting in children with acute gastroenteritis and emesis.[15]

DH is an ethanolamine group H1 antagonist with central nervous system (CNS) depressant, anticholinergic, antiemetic, antihistamine, and local anesthetic effects. Antiemetic action may result from inhibiting vestibular stimulation and acetylcholine. The most frequent side effect of first-generation H1 antagonists is sedation, drowsiness, and dizziness. Sedation can range from mild drowsiness to deep sleep.[16] The drug is used to control emesis and nausea after surgery in children as it is effective and safe. However, further studies are needed to demonstrate the effectiveness of DH in the control of vomiting in gastroenteritis patients.[17]

To date, there are no studies on DH effectiveness on the clinical condition of children with acute gastroenteritis in the Middle East. The aim of this study was to determine the effect of oral DH in controlling vomiting in acute gastroenteritis.

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Table 1: Characteristics of the study participants (n = 200).

Characteristics	Treatment group, n (%)		*p*-value
	Placebo (n = 100)	Dimenhydrinate (n = 100)	
Age (months)*	32.1±28.7	28.7±20.4	0.305
Male	45 (45%)	51 (51%)	0.479
Female	55 (55%)	49 (49%)	
Weight (kg)*	13.0±4.3	12.1±4.5	0.176

**Data given as mean ± SD. SD: Standard deviation.*

METHODS

This double-blind clinical trial was conducted in Mohammad Kermanshahi Hospital (a pediatric university-affiliated hospital in the western province of Iran) between August 2014 and March 2015. Samples were chosen from available patients admitted for gastroenteritis with mild to moderate dehydration and vomiting.

Patients were randomized into case and control groups (100 patients in each group) and received DH or a placebo drug, respectively. All participants in the study were blinded to selected group until the end of the data analysis. Inclusion criteria included patients diagnosed with gastroenteritis with at least five episodes of vomiting in the preceding 12 hours in children aged one to 12 years old. Patients were excluded if they had underlying chronic medical conditions (intestinal or stomach diseases, malignancy, metabolic disorders, cardiac diseases, endocrine diseases, immune system problems, and nervous system diseases), probable other diagnosis (the need for abdominal surgery, gynecological problems, urinary tract infection, migraine or meningitis), a history of chronic allergy or adverse reaction to hydrinate, severe dehydration requiring immediate intravenous fluids, and hematemesis or hematochezia. Patients were also excluded if they had taken any drugs, including antiemesis or anti-nausea drugs, other than acetaminophen or ibuprofen in the preceding 48 hours.

The study was explained to all parents, who gave their informed consent. The study was registered at the Iranian Registry of Clinical Trials.

DH was prescribed as four doses of 1 mg/kg every six hours (maximum 200 mg) and coded as A. The placebo was coded as B. Twenty-four hours after the first dose, patients were evaluated and the data was collected. The second step of data collection was at days seven and 14 after discharge and was obtained from the children's parents.

The primary outcome variable was treatment failure, defined as the occurrence of more than two episodes of vomiting in the 24 hours after the first dose. The secondary outcome was the number of episodes of diarrhea in one day and the duration of diarrhea. We also looked the presence of any side effects 24 hours after the first dose, the duration of hospitalization, the need for a second visit within seven days, and parent's satisfaction seven and 14 days after discharge.

RESULTS

A total of 200 children with acute gastroenteritis were enrolled in the study (104 female and 96 male). One-hundred patients were treated with DH, and 100 patients were treated with a placebo drug.

The age, weight, and sex of children in both groups are summarized in Table 1. The age of the children ranged from one to 12 years old. Their mean age was 30.4±20.7 months. Their mean weight was 12.6±4.3 kg (range = 7–36 kg).

Descriptive qualities and a comparison of the primary outcome variables and secondary outcome variables in children with acute gastroenteritis in each group is summarized in Table 2. The average number of episodes of vomiting, duration of vomiting, and hospitalization of children with acute gastroenteritis in study groups was not statistically significant.

Across both groups, the mean number of vomiting episodes was 4.4±2.3 (range = 0–15). The mean duration of vomiting was 2.3±1.3 days (range = 0–10 days). The mean number of episodes of diarrhea was 8.8±3.3 (range = 0–20) with a mean duration of 3.9±1.7 days (range = 0–10). Thirty-six (18.0%) children experienced sedation, one (0.5%) child had an excitement problem, and 16 (8.0%) children experienced sleepiness. The remaining 147 (73.5%) of children had no side effects. The mean duration of hospitalization was 45.4±30.6 hours

Table 2: Descriptive qualities and comparison of primary and secondary outcome variables in the two groups.

Variable	Treatment group, n (%)		*p*-value
	Dimenhydrinate	Placebo	
Number of vomiting episodes*	4.4±2.5	4.4±2.1	0.581
Duration of vomiting (days)*	2.5±1.5	2.1±1.0	0.102
Number of diarrhea episodes*	7.4±3.2	10.1± 2.8	<0.001
Duration of diarrhea (days)*	3.3±1.8	4.4±1.3	<0.001
Adverse effects			
Sedation	36 (36%)	0 (0%)	<0.001
Excitement	1 (1%)	0 (0%)	
Sleepiness	16 (16%)	0 (0%)	
No adverse effects	47 (47%)	100 (100%)	
Duration of hospitalization (hours)*	45.0±28.9	45.8±32.1	
Revisiting			
Yes	60 (60%)	100 (100%)	
No	40 (40%)	0 (0%)	
Parents' satisfaction at seven and 14 days			
Low	13 (13%)	52 (52%)	
Intermediate	47 (47%)	46 (46%)	
High	40 (40%)	2 (2%)	

**Data presented as mean ± SD.*

(range = 6–168 hours). One hundred and sixty (80%) children required revisiting (i.e., the children needed physical examination because of recurrent vomiting).

We also measured the parents' satisfaction rate at seven and 14 days after discharge: 65 reported low-level satisfaction, 93 a medium level, and 42 a high level. Twenty-four parents were unavailable.

There was no significant difference between the age, sex, and weight of children with acute gastroenteritis between the study groups ($p \geq 0.050$). The average number of episodes of diarrhea, diarrhea duration, side effects, the requirement for revisiting patients, and parents' satisfaction in both groups showed a significant difference ($p \leq 0.050$).

DISCUSSION

In our study, consumption of oral DH had no effect on the frequency and duration of vomiting in patients with acute gastroenteritis. This agrees with a study conducted in Canada in 2012,[18] but disagrees with the results obtained in Germany by Uhlih et al,[19] in 2009. The most likely explanation for the agreement of our study with Gouin et al,[18] is that we both used the same dosage and oral DH in our patients. In our study, the mean number of episodes of diarrhea in the DH group was statistically significant ($p \leq 0.050$), unlike the study by Gouin et al.[17,18] This discrepancy could be due to differences in physical, racial, social, and other conditions between the patients included in studies. In our study, the consumption of DH was effective for the number of episodes and duration of diarrhea experience in children with acute gastroenteritis, which could be due to a mild anticholinergic effect of DH. The use of antimotility agents is contradicted in children with dysentery.[3] Because the aim of this study was to evaluate the antiemetic effect of DH in acute gastroenteritis, patients were not matched for frequency and duration of diarrhea and, as a secondary outcome, the number of diarrhea episodes and duration of diarrhea were measured.

We do not recommend the use of DH as an anti-diarrhea drug, but our results showed a decrease in number and duration of diarrhea in our patients without serious effect. In the DH group, 36% of patients had a sedation problem, 16% had sleepiness (deep sedation) problem, and 1% had an excitement problem. The other 47% of patients reported no side effects. The difference in the side effects between the DH and placebo group was significant ($p \leq 0.050$). The antihistamine effects of DH could be attributed to the sedation effects we observed.

The average period of hospitalization between the two groups was not statistically significant, in line with the results of other studies.[17,19]

In children treated with DH, 60% needed revisiting and 100% of children treated with placebo needed revisiting. This difference could be due to the effectiveness of DH in reducing the frequency and duration of diarrhea. This could be the reason high parental satisfaction was recorded in 40% of children treated with DH and only 2% of children treated with placebo.

CONCLUSION

The consumption of DH has no effect on frequency and duration of vomiting, but our results showed

consumption of DH in acute gastroenteritis patients was effective in decreasing the frequency and duration of diarrhea. However, our two groups were not matched for these variable. We do not recommend the use of DH as an anti-diarrhea agent, but as it is a safe over-the-counter drug it could be investigated as an agent to reduce the duration of diarrhea.

Disclosure
The authors declared no conflicts of interest. This trial was registered at Iranian Registry of Clinical Trials (www.irct.ir) IRCT registration number: IRCT2014083018794N1.

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