Research Article

Assessment of effectiveness of nonspecific antidiarrheal agents in reducing the need for intravenous rehydration in children with acute diarrhea

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Abstract

Background: In clinical practice, nonspecific antidiarrheals are most commonly used by clinicians along with routine treatment to hasten the recovery and to give psychological reassurance. This study was conducted to assess the effectiveness of nonspecific antidiarrheal agents in reducing the need for intravenous rehydration in children with acute diarrhea. **Materials and Methods:** This was a prospective, observational study done in clinical settings for a period of 3 years at two pediatric clinics and at a tertiary care hospital. Children were divided into 5 treatment groups (viz, control, racecadotril, Mebarid, Diarex and loperamide) at the discretion of the pediatrician. One questionnaire was provided to parents to record the details about the course of diarrhea. Parents were sensitized to report any episode of complication or need for intravenous fluids. **Results:** The unscheduled need for intravenous fluids due to dehydration was significantly higher in control group compared to other groups {Control: 7.37%, Racecadotril : 1.71% Mebarid: 2.4%, Diarex: 0%, Loperamide : 0%)}. **Conclusion:** Present study suggests that use of nonspecific antidiarrheals may decrease the need for admission for intravenous fluids in children with acute diarrhea.

Key words: Acute diarrhea, Diarex, Loperamide, Mebarid, Nonspecific antidiarrheals, Racecadotril

Introduction

Acute diarrhea accounts for significant morbidity and mortality in children [1]. It is also a cause of anxiety and economic burden to parents of affected children as well as the nation. In developing countries it is mostly infectious in origin and is very often self limiting. Acute diarrhea is defined as diarrhea occurring within a minimum period of 24 hours and lasting usually for less than 7 days [1].

Antimicrobial agents have limited role as most episodes of diarrhea are caused by viruses and enterotoxigenic E.coli. Antibiotics do not alter the course of illness [2, 3]. ORS forms the mainstay in treatment of diarrhea [2-4]. Its use prevents and corrects dehydration, reduces the morbidity and mortality; but it does not reduce frequency & volume of stools or the duration of diarrhea [3].

Therefore, an effective anti-diarrheal treatment to prevent / reduce dehydration by reducing the frequency and duration of diarrhea would be beneficial. Hence, in clinical practice, nonspecific antidiarrheals (allopathic and ayurvedic) are commonly used by clinicians along with routine treatment, to hasten the recovery and to provide psychological relief [5-7]. Although they are used extensively in clinical practice, there are variable opinions and reports regarding their effectiveness [5-9].

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It is unclear whether use of these drugs leads to reduced need for IV rehydration as very few studies have considered this outcome. Hence, the present study was planned to assess whether the use of non-specific anti-diarrheal agents leads to reduction in the need for intravenous rehydration.

In our pilot study, it was observed that racecadotril, loperamide, Mebarid, and Diarex were the most commonly advised nonspecific antidiarrheals. Therefore,these agents were included in the study.
Mebarid, a polyherbal preparation contains Bael, Ajmoda, Lodhara, Dadim, Badishep, Daruhalad, Jaiphal, Sunth, Ativis and Kuda. Diarex is a herbomineral ayurvedic preparation containing Kuda, Guduchi, Bael Dadim, Shankh bhasma and Musta.

Materials and Methods

Settings: This was a prospective, observational study done in clinical settings for a period of 3 years. The study protocol was approved by Institutional Ethics Committee of MIMER Medical College, Talegaon, Pune. It was conducted at following centres after obtaining their permission

1. Pediatric clinic (secondary care hospital), Talegaon, Pune, Maharashtra.
2. Pediatric clinic (secondary care hospital), Chakan, Pune, Maharashtra.
3. Tertiary care hospital, Talegaon, Pune, Maharashtra.

The purpose of the study was explained to the concerned pediatricians and concerned authorities.

Study population and study design: Children suffering from acute diarrhea and fulfilling the selection criteria (Table 1) were enrolled into the study. Then parents of children were informed about the study in simple and lucid language. Informed written consent was obtained from parents of the children. Ascent was obtained from children between 7 to 10 years. Baseline demographic and clinical charecteristics were recorded which included- Age, weight, immunization status, history of fever, vomiting, or other symptoms, prior use of any medication, diarrhea duration, frequency, character of stools (watery, mucoid, bloody etc), consistency of stool, dehydration status etc.

Children were divided into 5 treatment groups at the discretion of the pediatrician. All children received oral rehydration therapy (ORT) and one of the nonspecific antidiarrheal drugs included in the study (Table 2). The antidiarrheals were prescribed till recovery. Control group consisted of patients who did not receive any nonspecific antidiarrheal in addition to oral rehydration therapy. Exclusion criteria are shown in table 3.

Table 1: Inclusion criteria

1. Age: 2 - 10 years.
2. Acute diarrhea of varied etiology.
3. Duration of diarrhea of < 2 days.
4. Diarrhea with mild co – morbidity.
5. No h/o of treatment with antimicrobials/antidiarrheals/antimotility drugs within the preceding 7 days.

Table 2: Details of treatment received by children during study

Drug	Dosage foms	Dose	Frequency
ORS (new formula hypoosmolar ORS)	Powder	as per WHO guidelines	as per WHO guidelines
Racecadotril	Tab, sachets	1.5 mg/kg/dose	Thrice daily
Mebarid	Liquid	<5 y 5ml twice daily >5 y 5ml thrice daily	Thrice daily
Diarex	Tab	<5 y 1/2 tab twice daily. >5 y 1 tab twice daily	Thrice daily
Loperamide	Tab	0.25 mg/kg/day 2-5y;Max3mg/d 6-8 y; Max 4 mg/d 8-10 y; Max 6 mg/day	Thrice daily

Table 3: Exclusion criteria

1. Age < 2 and > 10 years.
2. Iatrogenic / bloody diarrhea / or severe diarrhea e.g. cholera.
3. Diarrhea with severe dehydration / significant systemic illnesses.
4. Children with severe malnutrition (BW<50% of expected for that age)
5. Children receiving pre / probiotics and / or zinc supplements or any other nonspecific anti-diarrheal drug not

Data collection and data analysis: Prescription audit was conducted and prescriptions were analyzed in detail. Administrations of concomitant medications such as antipyretics, antiemetics were recorded. A questionnaire was provided to parents and they were instructed to fill and record the details of the diarrheal episodes till recovery. All the information was recorded in a predesigned CRF (Case Report Form) including the details of treatment drugs, which was filled on enrollment day in detail and on follow up days. Follow up was done on 3rd, 5th and 7th day of treatment. In cases of failure to follow up, personal visit was done by investigator. A telephonic check was carried out daily. Any episode of complication or need for unscheduled use of intravenous fluids was recorded.

Statistical analysis: Statistical analysis was done by appropriate methods using SPSS version 17 and primer of biostatistics. Data obtained are expressed as mean ± SEM. P<0.05 was considered as significant.

Results

600 patients were enrolled and out of which 584 successfully completed the study as per the protocol. Sixteen patients did not turn for the follow up; however, telephonic feedback was obtained successfully. Hence the data has been expressed of all 600 patients. Overall compliance in our study was good (90%). The base-line parameters are shown in Table 4. There was no significant difference between two groups.

Table 4: The base-line parameters of patients in the study

Parameters	**Control (n=190)**	**Racecadotril (n=175)**	**Mebarid (n=123)**	**Diarex (n=78)**	**Loperamide (n=34)**
Age(y)	4.79±0.16	4.16±0.14	4.43±0.20	7.05±0.19 *	7.65±0.26 *
Sex (M:F)	103:87	84:91	54:69	40:38	19:15
Weight (Kg)	16.07±4.24	15.03±3.62	15.45±4.47	20.54±3.32*	21.59±3.06*
Fully immunized Partially immunized	133 (70) 57 (30)	143 (82) 32 (18)	93 (76) 30 (24)	55 (71) 23 (29)	28 (82) 6 (18)
No dehydration Some dehydration	102 (54) 88 (46)	78 (45) 97 (55)	69 (56) 54 (44)	31 (40) 47 (60)	20 (59) 14 (41)
Duration of diarrhea before enrolment (h)	45.16±1.13	41.55±1.27	42.24±1.34	40.61±1.70	39.84±2.35
Frequency of stools/day	4.98 ±0.12	5.18 ±0.14	5.27 ±0.17	5.49±0.21	5.68±0.30
Vomiting (No.of children)	24 (13)	18 (10)	26 (21)	9 (12)	5 (9)
Fever (No.of children)	35 (18)	21 (12)	11 (9)	14 (18)	3 (9)
Comedication: Antiemetics Antpyretics (No.of children)	 12 (50) 21 (60)	 8 (44) 15 (71)	 19 (73) 10 (91)	 6 (67) 10 (71)	 5 (100) 2 (67)
Antibiotics for co-morbidity (No.of children)	40 (21)	37 (21)	30 (24)	25 (32)	4 (12)
Values are mean ± SEM. Figures in parenthesis indicate percentage.					

Table 5: Distribution of children according to intravenous rehydration in various study groups

Group	Need for intravenous rehydration	
	Given (%)	Not given (%)
Control	14 (7.37) *	176 (92.63)
Racecadotril	3 (1.71)	172 (98.29)
Mebarid	3 (2.40)	120 (97.60)
Diarex	0	78 (100)
Loperamide	0	34 (100)
Total	20 (3.33)	580 (96.67)

$P < 0.005$

In all the children given various antidiarrheal drugs, the need for intravenous rehydration was significantly less as compared to those in control group (Table 5).

The unscheduled need for intravenous fluids due to dehydration was significantly higher in control group (7.37%) compared to all other groups treated with non-specific anti-diarrheal agents. In current study, we have compared control group with other groups. No intergroup comparison has been made.

Only 1.71% children needed unscheduled intravenous. intervention in racecadotril group compared to 7.37% children in control group; indicating that racecadotril reduced the admissions needed for intravenous rehydration.

Discussion

In a hospital based study by Manfredi M et al (2013) [10] in children, 26.9% in the racecadotril supplemented group and 42.9% in ORS group needed i.v. rehydration due to dehydration respectively. This was a retrospective study with a small sample size (n=61) conducted in a primary care hospital and included children with mild to moderate dehydration. The reason cited for parenteral therapy in these children was worsening and persistence of symptoms. However in present study, comparatively very few children (1.71%) in racecadotril group needed intravenous rehydration. The difference observed might be because of differences in patient population.

In the present study, no child on loperamide needed unscheduled IV intervention indicating that loperamide was very effective in preventing the need for i.v.rehydration.

Very few children (2.4%) on Mebarid required i.v. intervention compared to control. No patient from Diarex group required hospitalization for i.v. intervention indicating that supplementation of Diarex reduced the need for hospitalization for i.v. rehydration therapy. The decrease in frequency and duration of diarrhea resulting from administration of these non-specific anti-diarrheal agents might be responsible for the reduced need for intravenous rehydration. This may result in decrease in the cost of trearment and allay the anxiety associated with hospitalization. Very few studies are available in literature on these antidiarrheals assessing this clinically and economically important outcome measure. Further multicentric studies are necessary to assess the efficacy and safety of such agents in large population of patients.

Conclusions

Present study suggests that use of nonspecific anti-diarrheals leads to decrease in the need for admission for intravenous fluids in children with acute diarrhea. Hence,it may be appropriate to use such drugs in management of acute diarrhea in children.

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Permission of IRB: Yes

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