

ORIGINAL RESEARCH

Comparative efficacy of antidiarrheal activity of DIAREX, an ayurvedic antidiarrheal formulation vs. loperamide in children with acute diarrhea

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ABSTRACT

In clinical practice, nonspecific antidiarrheals (allopathic and ayurvedic) are commonly used by clinicians along with routine treatment to hasten the recovery and to give psychological reassurance. Although they are used extensively in practice, studies comparing their efficacy are few. This prospective observational study was carried out at two private clinics run by pediatricians to compare the efficacy, safety, and tolerability of DIAREX, an ayurvedic antidiarrheal formulation versus loperamide in the treatment of acute diarrhea.

Children aged 5y to 10 y who presented to the clinic with acute diarrhea and fulfilling selection criteria were enrolled and divided into two treatment groups viz, DIAREX and loperamide. Data collection was done using predesigned case report forms and questionnaires. Outcome Measures used were 1)Duration of diarrhea, after initiation of treatment 2)Frequency of stools until recovery 3)Time required for improvement in stool consistency. The groups were comparable clinically and demographically at enrolment.

Loperamide improved stool consistency in less time compared to DIAREX (16.24h vs 29.00h). Patients on loperamide passed 3.32 ± 0.16 stools before recovery, while patients on DIAREX passed 5.26 ± 0.27 stools. Rapid improvement in stool consistency and frequency was found with loperamide compared to DIAREX. The mean duration of diarrhea was less for loperamide group (30.35 ± 1.43 h Vs. 42.77 ± 1.48 h; $P < 0.05$).

DIAREX was found to be clinically useful to decrease the duration and symptoms in acute diarrhea in children. However, loperamide was more effective. DIAREX may be used, if there is concern about the adverse events with loperamide.

Key words: Acute diarrhea, Loperamide, DIAREX, Nonspecific antidiarrheals, Children

INTRODUCTION

Acute diarrhea is major cause of childhood morbidity and mortality. In developing countries, in which the toll of diarrhea is highest, poverty also adds an enormous additional burden, and long-term consequences of the vicious cycle of enteric infections, diarrhea, and malnutrition are devastating.

Acute diarrhea is defined as history of at least three loose or watery or unformed stools in a minimum period of 24 hours and usually for the duration of less than 7 days.¹ Acute diarrhea in children is very often self-limiting within few days.²

Antibiotics play very limited role and do not alter the course of illness.^{3,4} However, children are prone to develop dehydration and complications. ORS forms mainstay in treatment of diarrhea;⁵ but ORS does not reduce frequency & volume of stools or the duration of diarrhea. An effective antidiarrheal which reduces the frequency and duration of diarrhea is needed and it will also give psychological reassurance to patients / parents. Therefore, the World Health Organization has recommended that drug treatment be added to rehydration therapy, as long as the drug used has proven safety and efficacy in the pediatric population.⁶ Hence, in clinical practice, nonspecific antidiarrheals like loperamide and DIAREX (allopathic and ayurvedic) are commonly used by clinicians along with the routine treatment so as to hasten the recovery and to give psychological reassurance to patients / parents.^{7,8,9}

Loperamide is widely used in adults for acute diarrhea. However its use in children is mostly discouraged owing to concerns over safety. It is a μ receptor agonist, opiate with antimotility action.

Although loperamide is accepted antidiarrheal agents in allopathy, not many reports were found in literature regarding time required for improvement in stool consistency. Again, several studies about this drug have been reported in the literature comparing its efficacy with racecadotril, no study has been reported in our country comparing its efficacy with DIAREX, a commonly used ayurvedic antidiarrheal in clinical practice in India. Hence, this study was designed to compare the efficacy, safety and tolerability of DIAREX and loperamide in the treatment of acute diarrhea in children.

DIAREX is a herbomineral ayurvedic preparation in which herbs are mixed with shankha bhasma and is available in tablet form. Diarex contains Kuda, Guduchi, Bael, Dadim, Shankh bhasma, Musta. This DIAREX formulation was tested for efficacy in adults in treatment of diarrhea.¹⁰ Efficacy studies in children are few and were small and not scientifically planned.¹¹ Studies carried out on ayurvedic preparations like DIAREX claim that it does not have any adverse effect.^{10,11} The purpose of this study is also to find out whether these preparations are really free of adverse effects as claimed.

AIMS AND OBJECTIVES

To compare the efficacy, safety, and tolerability of DIAREX versus loperamide in the treatment of acute diarrhea in children.

MATERIALS AND METHODS

Settings: This was a prospective, observational study done in clinical settings for a period of 18 months. Two private clinics, run by registered medical practitioners (pediatricians), were selected after obtaining their informed written consent.

ETHICS COMMITTEE APPROVAL

The study protocol was approved by Institutional Ethics Committee of MIMER Medical College, Talegaon, Pune, Maharashtra.

STUDY POPULATION

Children suffering from acute diarrhea presenting with 3 or more unformed stools in 24 hours and fulfilling the selection criteria (Table1) were enrolled in the study. Informed written consent was obtained from one of the parents. They were divided into two treatment groups- loperamide and DIAREX at the discretion of pediatrician. Both groups were treated with

routine antidiarrheal drugs, while loperamide group received loperamide in addition, DIAREX group received DIAREX in addition.

Baseline demographic and clinical characteristics were recorded.

Following baseline data were collected: Age, weight, immunization status, history of fever, vomiting, degree of dehydration (No, some) or other symptoms, prior use of any medication were noted.

Duration of diarrhea, character of stool (watery, mucoid, bloody etc), consistency of stool, were noted. A child could be enrolled only once.

DATA COLLECTION AND DATA ANALYSIS

Children suffering from acute diarrhea attending the clinic were examined by the pediatrician first. Case history was obtained followed by clinical examination. Prescription audit was conducted and prescription was analyzed in detail. Administration of concomitant medications such as antipyretics, antiemetics were recorded. Parents of children were informed in detail the study protocol in simple and lucid language.

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, adverse effect or need for unscheduled use of IV fluids was recorded. Parents were sensitized to report the adverse effects like abdominal distension, drowsiness, lethargy, vomiting or constipation as early as possible.

OUTCOME VARIABLES

Efficacy criteria:

1. The primary efficacy criterion was duration of diarrhea- time between initiation of treatment and production of the final diarrheal stool.¹²
2. Secondary efficacy criteria consisted of frequency of stools after initiation of treatment until recovery and time needed for improvement in stool consistency.^{13,14}

Tolerability and safety were evaluated by recording the adverse effects experienced during treatment.

Recovery was defined as

1. Production of two consecutive normal stools
2. Production of one normal stool followed by 12 hours with no stool production.
3. No stool production for a period of 12 hours⁷

STATISTICAL ANALYSIS

Statistical analysis was done using the SPSS (Statistical Package for the Social Science) Version 17 for window. Statistical analysis was done using Student's unpaired "t" test, ANOVA, Chi-square, Post hoc Tukeys test as required. All the values are expressed as mean \pm SEM. P<0.05 was considered as significant.

RESULTS AND DISCUSSION

Total 112 children were enrolled, 34 in loperamide group and 78 in DIAREX group. Both the groups tolerated the treatment well and continued the medications as advised till the end of treatment. Compliance in our study was quite good. The base-line parameters are shown in table 2. There was no significant difference between two groups.

ASSESSMENT OF EFFICACY

There was significant difference in time needed for improvement in stool consistency between loperamide and DIAREX (16.24h vs.29.00h; $P < 0.05$). Thus loperamide improved stool consistency in less time compared to DIAREX. Patients on loperamide passed 3.32 ± 0.16 stools before recovery, while patients on DIAREX passed 5.26 ± 0.27 stools. This indicates loperamide was more effective in reducing frequency of stools compared to DIAREX. The mean duration of treatment was less for loperamide group (30.35 ± 1.43 h Vs. 42.77 ± 1.48 h; $P < 0.05$). Addition of loperamide significantly reduced the duration of diarrhea (Table 3)

SAFETY EVALUATION

Of the 112 patients studied, no severe adverse events were observed in children. Overall adverse events in both loperamide (17.65%) and DIAREX ((17.95) groups were comparable.

5 patients from loperamide group complained of abdominal pain which was relieved by appropriate drugs and only 1 patient complained of drowsiness. This CNS related adverse event was not observed with non-allopathic antidiarrheal DIAREX. 5 patients complained of vomiting and 9 patients complained of fever in DIAREX group. There was significant difference observed in incidence of the adverse event abdominal pain between these study groups i.e. $P < 0.05$. No serious adverse effects were recorded during the study (Table 4).

Present study examined several aspects of loperamide and DIAREX supplementation. Moreover, the stool consistency and frequency, which are primary concerns of the parents are taken care of by both these drugs. Both these drugs resolved the symptoms of acute diarrhea rapidly and effectively. A decline in the frequency and an improvement in stool consistency was noted within 24 hrs after the initial visit in loperamide group. As is seen that the diarrheal duration was comparable in both groups initially, but after treatment, loperamide supplemented group has shown faster recovery. The duration of diarrhea was significantly shorter with loperamide (30.35h; $P < 0.05$) compared to DIAREX (42.77h).

However the symptomatic relief seen with these non-specific antidiarrheals may reduce suffering of parents and caretakers to a large extent. Difference in two groups is probably because of presence of multiple ingredients in DIAREX (nonallopathic antidiarrheal) having multiple actions in contrast to allopathic drug loperamide which has specific action. Improvement in symptoms and severity of acute diarrhea occurring because of use of these drugs may be acceptable and desirable by the parents of children. This might also improve the use of ORS which forms the mainstay of treatment of diarrhea.

The results obtained in the present open label study are preliminary in nature and require further scientific studies with larger sample size. This study did not take into consideration other associated symptoms.

CONCLUSION

In this comparative study, DIAREX was found to be clinically useful to decrease the duration and symptoms in acute diarrhea in children. However, loperamide was more effective. DIAREX may be used, if there is concern about the adverse events with loperamide.

Table 1: Selection criteria

Inclusion Criteria for enrollment was as follows:

1. Age: 5 - 10 years
2. Acute Diarrhea of varied etiology
3. Duration of diarrhea of less than 2 days.
4. Diarrhea with co - morbidity which is not severe.

Children were excluded from the study based on following criteria:

1. Children less than 5 yrs and above 10 yrs.

2. Chronic, iatrogenic or bloody diarrhea.
3. Children with severe diarrhea and severe dehydration.
4. Children with severe malnutrition.
5. Children receiving antibiotics, pre/probiotics and/or zinc supplements or any other nonspecific anti-diarrheal drug.
6. Child with any other significant systemic illnesses

Table 2: Base-line parameters of patients on enrolment

Sr. No	Particulars	DIAREX	Loperamide
1	Number of children	78	34
2	Age (y)	7.05 ± 0.19	7.65 ± 0.26
3	Sex (M:F)	40:38	19:15
4	Body weight (kg)	20.54 ± 0.38	21.59 ± 0.53
5	Immunization status		
	Fully Immunized (%)	55 (71)	28 (82)
	Partially Immunized (%)	23 (29)	6 (18)
6	Dehydration		
	No Dehydration	47	14
	Some Dehydration	31	20
7	Duration of diarrhea before enrolment (h)	40.62 ± 1.70	39.88 ± 2.36
8	Frequency of stools/day	5.49 ± 0.21	5.68 ± 0.30
9	Vomiting (No.of children)	09	05
10	Fever (No.of children)	14	03

Values are mean ± SEM

Table 3: Efficacy of DIAREX and loperamide

Group	DIAREX (n=78)	Loperamide (n=34)
Time(h) needed for improvement in stool consistency	29.00 ± 1.32	16.24 ± 1.20 ***
Stool frequency	5.26 ± 0.27	3.32 ± 0.16 ***
Duration of diarrhea	42.77 ± 1.48	30.35 ± 1.43 ***

Values are mean ± SEM

*** $P < 0.05$ compared with DIAREX

Table 4: Details of adverse event wise distribution of children in study groups

Group	DIAREX	Loperamide	P value
	n=78	n=34	
Vomiting	5(6.41)	0	> 0.05
Fever	9(11.54)	0	< 0.05
Abd. Pain	0	5 (14.71)	< 0.05
Drowsiness	0	1 (2.94)	-
Headache	0	0	-
Rash	0	0	-
Others *	0	0	-

*Others means nausea, weakness, bodyache, irritability, excessive crying etc.

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CONFLICT OF INTEREST

Nil

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