

Loperamide in Adult Acute Diarrhea

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ABSTRACT •

Introduction: Decrease in duration of diarrhea significantly reduces morbidity, loss of working days, hospital bed occupancy and use of hospital resources. Loperamide is an established treatment of acute diarrhea to decrease the duration and frequency of unformed stool with only rare adverse reactions.

Methods: This is a descriptive, cross sectional, parallel group, single centre study done in odd and even days of the month for treatment and control group. The study was conducted from 1st to 30th September 2010 in Patan Hospital Emergency Department.

Results: Out of 104 patients, 43 patients were included in Loperamide group and 63 patients were taken in supportive treatment group. Mean duration of diarrhea was 16.3 and 41.9 hours in supportive plus Loperamide group and supportive treatment only group respectively. Mean difference in duration of diarrhea was 25.6 hours 95% CI (23.9 to 27.3) ($P < 0.05$). Similarly mean working day loss was 1.19 in group treated with Loperamide and 2.84 days in group not treated with Loperamide. Mean difference was 1.65 days CI 95% (1.45 to 1.85) ($P < 0.05$). Absolute risk of complication in Loperamide group was 6.6%

Conclusion: Loperamide significantly reduces duration of diarrhea and working days lost with low rate of complications in Adult with acute non infective diarrhea.

Keywords: *Loperamide and diarrhea; non infective diarrhea*

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INTRODUCTION

Diarrhea is defined as stool weight in excess of 200 grams per day. However, this definition is of little clinical value, since collecting and weighing stools is not practical in our setup. A good working definition is three or more loose or watery stools per day or a definite decrease in consistency and increase in frequency based upon an individual baseline. Diarrhea can further be classified as acute for loose stool lasting less than 14 days and persistent diarrhea if loose stool lasting more than 14 days. Diarrhea lasting more than 30 days is known as chronic diarrhoea.¹

Acute diarrhea is a common problem presenting to medical care. Diarrheal diseases represent one of the five leading causes of death worldwide.^{2,3} It accounts for more than two million deaths annually.⁴ In Nepal diarrhea is the second most common disease causing morbidity. Outbreak of diarrhea in April-June 2009 has caused significant morbidity and mortality in western Nepal.⁵

The mainstay of treatment is fluid therapy and correcting electrolyte disturbance. Antimicrobial therapy is only indicated in selected cases.⁶ Anti-diarrheal agents are frequently prescribed by clinicians. According to current guidelines, they are not recommended for routine use in children with acute diarrhea, because of potential side effects and doubtful benefits.^{7,8} However, in adults, their use is more liberal. There are many over-the-counter anti-diarrheal agents and quite often patients request anti-diarrheal drugs during their consultations. The current anti-diarrheal agent of choice is Loperamide.⁹

Diarrhea has shown to cause significant morbidity, loss of working days, increase in hospital bed occupancy and use of hospital resources. To decrease this Loperamide can be used as an adjunct to the treatment along with fluids and electrolytes replacement.

METHODS

This is a single centre, descriptive, cross sectional, parallel group study conducted in Patan Hospital, Emergency Department in the month of September 2010. Patient

coming on the odd days of the calendar month were given Loperamide and those patient coming on even days of month were taken given symptomatic treatment only. Patient more than 18 years with acute watery diarrhea were included in the study and those with chronic, iatrogenic, bloody diarrhea, having received antibiotics treatment or anti diarrheal drug in last five days, history of renal or hepatic dysfunction, immunocompromise, concomitant infection, lactating mother and patient with decompensate shock were excluded from the study. Written consent was taken from the patient. All patients in Loperamide group were informed about the medicine, its advantage and possible side effects. Time of onset of diarrhea with frequency was noted.

In this study acute diarrhea is defined as the passing of at least 3 watery stools in a minimum of 24 hours and for the duration of less than five days. Stable patient is defined as hemodynamically stable, tolerating orally and without ongoing loss. Recovery is defined as the production of 2 consecutive normal stools or no stool production for a period of 24 hours. The duration of diarrhea after treatment means the time between the Loperamide and the last loose stool. The first day of diarrhea means the 24 hours following the ER consultation, the second day means the 24 hours after the first day, and so on. Loperamide is available as 2 mg capsule and was given 2 capsules stat and then followed by 1 capsule after each loose stool but not more than 8 capsules in a day including the stat dose.

Patients were followed up by telephone on day 3 of discharge. In the telephone interview, the intake of medications, time of the last diarrhea, and the daily frequency of diarrhea after discharge was enquired. The primary end-points of the study are to determine significant difference in duration of diarrhea (Measured in terms of hours) following treatment in these two groups. Secondary end-points were to determine the number of working days lost.

Statistically analysis was done in SPSS 15.0 with Chi square test and comparison of means were done using student's T test..

RESULTS

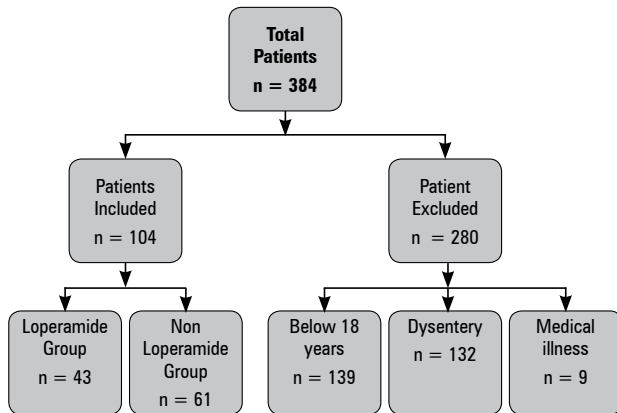


Figure 1. Flowchart showing the study profile

In non Loperamide group 45.9% were male and 54.1% were female, in Loperamide group 46.5% were male and 53.5% were female. Similarly in non Loperamide group 24.5% were from Kathmandu, 40% from Bhaktapur and 34.5% from Patan. In Loperamide group 23.2% were from Kathmandu, 37.2% from Bhaktapur and 39.6% from Patan. 37.3% were in age group < 35 years, 37.2% in age group >35<50 and 25.6% in age group > 50 years in non loperamide group. In Loperamide group 49% were in age group <35, 31% in age group >35<50 and 20% in the age group > 50 years. Mean age in Loperamide and non Loperamide group was 38.53 and 35.3 years respectively($p=0.02$). Total duration of diarrhea at the time of presentation in Emergency Department was 14.4 (SD 1.4) hours in Loperamide group and 13.3 (SD 1.25) hours in non Loperamide group ($P = 0.862$). Frequency of diarrhea at the time of presentation to emergency department is given below in table;

Frequency of Diarrhea	Non Loperamide Group	Loperamide Group
$\geq 3 < 10$	43	30
$\geq 10 < 20$	18	13

Table 1: Frequency of diarrhea on presentation to ER. Chi Square Significance $P=0.937$

Mean duration of diarrhea was 16.3 in the group treated with Loperamide and 41.9 hours in the group without Loperamide. Mean difference was 25.6 hours (95% CI 23.9 to 27.3) ($P<0.05$). Similarly working day loss was 1.19 in group treated with Loperamide and 2.84 days in control group. Mean difference was 1.65 days (95% CI 1.45 to 1.85) ($P<0.05$). Mean duration of diarrhea after Loperamide was 2.14 hours

Mean duration of diarrhea and working days loss in both groups is given below in table 3;

Age (Years)	Duration of Diarrhea (Mean hours)			Working days loss (Mean Days)		
	Non Loperamide Group	Loperamide Group	P value	Non Loperamide Group	Non Loperamide Group	P value
< 30 years	41.9	15.8	< 0.001	1.9	1.13	<0.001
>30 to < 50	41.4	17.2	< 0.001	1.58	1.25	<0.001
>50	41.9.	15.6	< 0.001	1.75	1.18	<0.05

Table 2: Comparison of mean duration of diarrhea and working days loss

Sex	Duration of Diarrhea (Mean hours)			Working days loss (Mean Days)		
	Non Loperamide Group	Loperamide Group	P value	Non Loperamide Group	Loperamide Group	P value
Male	41.9	15.8	< 0.001	1.9	1.13	< 0.001
Female	41.4	17.2	< 0.001	1.58	1.25	< 0.001

Table 3: Comparison of mean duration of diarrhea and working days loss

Variables		Duration of Diarrhea after Loperamide	P Value
Age (Years)	< 30	2.31	>0.05*
	>30 to <50	2.18	
	>50	2.14	
Sex	Male	2.15	>0.05
	Female	2.13	

Table 4: Comparison between age category and sex

*Age group < 30 years compared with other age group

Out of 43 patients in the group treated with Loperamide 11.6% (n=5) patient developed abdominal distension with cramps. Similarly 4.9% (n = 3) out of 61 patients in control group were also observed to have abdominal distention with cramps. Patients developing distention with cramp in both groups were in the age group > 50 years. Absolute risk of complications with loperamide was 6.6%

DISCUSSION

In this study, though randomization and placebo control trial was not done, the sample taken for both groups showed no statistically significant difference in terms of duration and frequency of diarrhea at the time of presentation to emergency department.

Practical guidelines for acute diarrhea published by the World Gastroenterology Organization (WGO) recommend Loperamide for self medication in otherwise healthy adults.¹⁰ But the research findings showed that half (48%) of GPs said they would rather use oral rehydration therapy alone and let diarrhea run its course.¹¹ The research also showed that the majority (69%) of diarrhea sufferers wanted a treatment that is fast acting. In Loperamide group, relief of diarrhea was significantly more rapid in our study. Loperamide significantly reduced the duration of diarrhea, 16.3 verses 41.9 hours in non Loperamide group. The mean difference was 25.6 hours which was consistent with two RCTs comparing Loperamide with a placebo. In first study (409 participants) mean duration of diarrhea was 27 hours in Loperamide group versus 45.25 hours in placebo group (p = 0.006). In second study (261 participants) mean duration of diarrhea was 17.5 hours in Loperamide group versus 37 hours in placebo group (p = 0.007).¹²

Age was categorically analyzed which showed a significant decrease in the duration of diarrhea in Loperamide group compare to non-Loperamide group in all age categories. Similarly this was true for male and female.

Average duration of diarrhea after Loperamide was 2.14 hours. This was also categorically analyzed in terms of age and sex which showed no significant difference between different age group and sex. In a study treatment with

Loperamide significantly reduced the average number of unformed stools in the first 4 hours after treatment.¹³

Similarly working day loss was 1.19 in group treated with Loperamide and 2.84 days in non Loperamide group. Mean difference was 1.65 days. "In times of economic uncertainty, people want to be productive in their working life, not have to take time off work, and carry on with their lives as normal. 76% of people agreed that diarrhea stops them from doing things they would normally do, so clearly, letting the diarrhea run its course is not always an option for many people."¹⁴

In Loperamide group 5 patients and in control group 3 patients developed abdominal discomfort with cramps and these patients were in the age group more than 50 years. In a study by Hwang-Huei Wang et.al the adverse events of Loperamide was found as constipation 9%, bloody stool 1%, however other adverse events like abdominal pain on palpation, skin itching, palpitation, dizziness, cold sweating, and headache were not observed.¹⁵ In our study we did not observe constipation in any patient treated with Loperamide.

CONCLUSION

Loperamide reduces the duration of diarrhea and also decreases the working days lost without significant complications. People who suffer from acute diarrhea should be recommended to maintain adequate fluid intake, diet as tolerated and Loperamide as required, so that they can get on with their lives. However, a further randomized placebo controlled trials are required to verify the result in our setup as RCT's published are from the western part of the world.

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