

## Lactose-Free Compared with Lactose-Containing Formula in Dietary Management of Acute Childhood Diarrhea

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### Abstract

**Objective:** Few reports are available on some benefits, such as shortened duration of diarrhea and better weight gain, for lactose-free over lactose-containing formula in acute childhood diarrhea. We evaluated the effects of lactose-free formula in dietary management of acute diarrhea in formula-fed children.

**Methods:** This controlled-clinical trial was conducted on formula-fed children, aged 1 to 24 months, referring with acute non-bloody diarrhea ( $\leq 2$  weeks). Those who had major systemic illness, severe malnutrition, severe dehydration, severe vomiting, or history of antibiotic therapy were not included. Children were allocated to receive lactose-free formula (intervention, n=37) or lactose-containing formula (control, n=34). Time to diarrhea relief and weight change were compared between the two groups after one week.

**Findings:** During the study, 32 male and 39 female children ( $7.1 \pm 3.7$  months) were included. Those who received lactose-free formula had a significantly shorter time to diarrhea relief compared with the controls ( $1.7 \pm 0.7$  vs.  $2.6 \pm 0.7$  days,  $P < 0.001$ ). Weight significantly increased in both groups, but there was no difference between the two groups in weight change ( $37 \pm 100$  vs.  $38 \pm 77$  gr,  $P = 0.673$ ). Multivariate analysis showed that receiving lactose-free formula significantly predicted time to diarrhea relief (95% CI: 1.5 to 3.9,  $P < 0.001$ ) controlling for baseline characteristics.

**Conclusion:** Early administration of lactose-free formula for formula-fed children presenting with acute diarrhea can result in a more rapid relief of acute diarrhea and thus perhaps less mortality and morbidity. Trials with longer follow-ups are warranted to better evaluate long-term results such as weight change and feeding problems in this regard.

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**Key Words:** Acute Diarrhea; Nutritional Management; Children; Lactose-Free Formula

### Introduction

Acute diarrhea still remains a leading cause of mortality and morbidity in children of the developing countries [1]. The appropriate management of acute childhood diarrhea consists of fluid and electrolyte therapy, suitable

antibiotics (e.g. in case of shigellosis, severe cholera, etc.), and adequate nutritional therapy [2-4]. Greater attention to nutritional therapy is particularly important in developing countries, where evidence showed a significant association between the prevalence of diarrhea and children's growth increments [5]. If remained un-controlled,

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prolonged acute diarrhea can reduce growth and increase risk of persistent diarrhea in children [6].

Benefits such as shortened duration of diarrhea, better weight gain, and ameliorating dehydration with a decreased need to intravenous fluid therapy were reported for lactose-free, compared with the lactose-containing formula, in formula-fed children with acute diarrhea [7,8]. Although benefits were reported for lactose-free formula and adverse complications seem to be more likely to occur in children who receive a milk diet containing lactose during acute diarrhea, there is still an argument for the use of a specifically designed lactose-free formula or its routine use for acute childhood diarrhea [9,10]. Moreover, few controlled studies are reported in this regard. Therefore, we evaluated the effects of early administration of the lactose-free formula compared with continuing lactose-containing formula in the management of acute diarrhea in formula-fed children under two years old.

## **Subjects and Methods**

### **Patients and setting**

This controlled-clinical trial was conducted from January 2009 to August 2009 in the pediatrics clinics at two referral University Hospitals in Isfahan (Iran). Formula-fed children, aged 1-24 months, with acute non-bloody diarrhea ( $\leq 2$  weeks) were enrolled consecutively in the study. Children who had mucous bloody stools, major systemic illness, severe malnutrition (weight for age  $< 60\%$  and/or weight for height  $< 70\%$ ), severe dehydration requiring intravenous infusion, severe vomiting, or history of antibiotic therapy were not included. The required sample size was calculated as 37 subjects in each group considering  $\alpha = 0.05$  and study power = 0.8 and expecting a difference of 1 day in duration of diarrhea. The Ethics Committee of Isfahan University of Medical Sciences approved the study protocol and written consent was obtained from all parents after full explanation of the study aim and protocol.

### **Interventions**

At admission time (first visit), after obtaining the demographic data and medical history, nude weight was measured with scale with an accuracy of 10g. Dehydration was assessed and oral rehydration therapy was performed according to World Health Organization (WHO) guidelines[2]. In children with mild dehydration, 50 ml/kg and in children with moderate dehydration, 100 ml/kg of oral rehydration solution (standard WHO-ORS) was prescribed during the first four hours. After the initial rehydration phase, for maintenance treatment, children were alternately allocated to receive 100 ml/kg/day of either lactose-free or lactose-containing formula. Children were discharged after confidence of tolerance of oral hydration, and the parents were explained about the red flags and asked to mention to consistency of stools at home and report on the days of follow-up. The second visit was done seven days after the first visit for measuring weight and evaluating time to diarrhea relief.

### **Outcomes and statistical analyses**

The time to diarrhea relief and nude body weight seven days after intervention were considered as outcomes. After gathering data, we used the independent sample t-test and Chi-Square test for comparisons. For data without normal distribution appropriate non-parametric tests were applied. *P* value of  $< 0.05$  was considered a statistically significant difference. Analyses were done using SPSS for windows (version 16.0).

### **Findings**

Three subjects in the control group did not participate for follow-up evaluations. Remained subjects were 32 male and 39 female children with mean age of  $7.1 \pm 3.7$  months. The two groups were similar in demographic and baseline characteristics except that the intervention group had more days with diarrhea at baseline ( $P=0.047$ ) and dehydration was more severe in the control group ( $P=0.015$ ); Table 1.

**Table 1:** Comparison of demographic and baseline characteristics between the two groups

Variable	Intervention n = 37	Control n = 34	P. value
Age (month)	7.6±3.9	6.6±3.4	0.3*
Gender Male	16 (43.2%)	16(47.0%)	0.5#
Female	21 (56.7%)	18(52.9%)	
Days with diarrhea at baseline	2.9±1.2	2.2±0.6	0.047 ‡
Dehydration Mild	35(94.5%)	25(73.5%)	0.02 #
Moderate	2(5.4%)	9(26.4%)	
Baseline Weight (kg)	6.5±1.9	6.4±1.9	0.8*

Data are shown as mean ( $\pm$  Standard Deviation) or number (%)

\* Independent *t*-Test

# Chi-Square Test

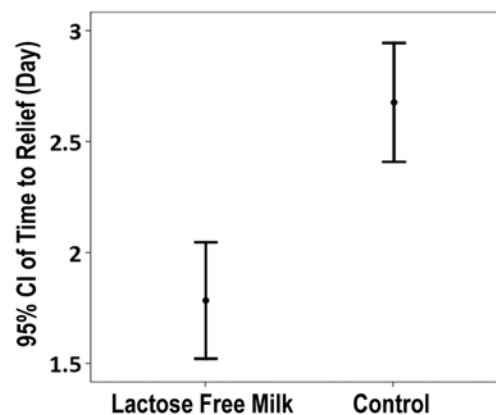
‡ Mann-Whitney Test

After therapy, those who received lactose-free formula had a significantly more rapid diarrhea relief compared with the controls ( $1.7\pm 0.7$  vs.  $2.6\pm 0.7$  days,  $P<0.001$ ); Fig. 1. Weight significantly increased in both the intervention ( $6.59\pm 1.94$  to  $6.63\pm 1.90$  Kg, [CI 95%: 4 to 71 gr]  $P=0.03$ ) and control ( $6.45\pm 1.99$  to  $6.49\pm 2.00$  Kg, [CI 95%: 11 to 65 gr]  $P=0.007$ ) groups, but there was no difference between the two groups in weight change ( $37\pm 100$  vs.  $38\pm 77$  gr,  $P=0.7$ ); Fig. 2.

Considering differences between the two groups before the intervention, we conducted a multivariate analysis, controlling for baseline values. Multivariate analysis showed that receiving lactose-free formula significantly predicted time to diarrhea relief (95% CI: 1.5 to 3.9,  $P<0.001$ ) while controlling for gender ( $P=0.3$ ), age ( $P=0.2$ ), dehydration ( $P=0.2$ ), and the baseline number of days with diarrhea ( $P=0.8$ ). It must be noted that one child in the intervention group experienced skin rash.

## Discussion

Current issues in dietary management of acute childhood diarrhea include the optimal timing of introduction of foods during illness, the appropriate use of milk-containing treatment regimens, mixed diets containing common staple foods, and the proper use of specific micronutrient supplements<sup>[2]</sup>. The aim of our study was to evaluate the effectiveness of early administration of lactose-free milk formula in the management of acute diarrhea in formula-fed children. We found a significant reduction in the period of diarrhea in children with acute diarrhea who received lactose-free compared with the lactose-containing formula. However, we did not find any difference with regard to weight changes after therapy. Our result was supported with some previous studies. Xu and Huang found a significantly shorter duration for diarrhea remission ( $3.17\pm 1.04$  days) in the lactose-free formula group compared with



**Fig. 1:** Comparison of diarrhea relief time between the two groups

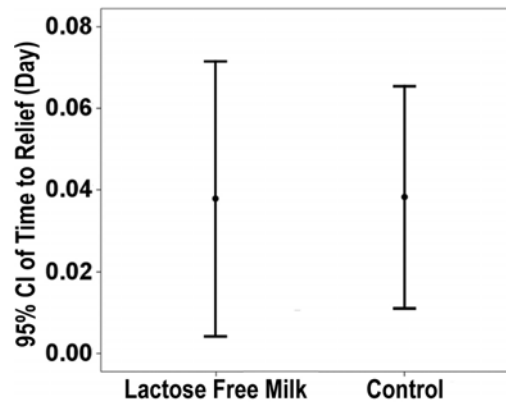


Fig. 2: Comparison of weight change between the two groups

conventional formula group ( $5.25 \pm 1.58$  days) [7]. In another study, Simakachorn and colleagues found that the median duration of diarrhea was significantly shortened by 20.5 hours in the lactose-free diet group compared to the control group. They also found significantly higher weight gaining in children with lactose-free diet compared with the control group [8]. Wall and colleagues in a randomized trial compared the efficacy of a low-lactose hydrolyzed milk formula, a lactose-free corn syrup-based milk formula, and a standard lactose-containing formula during re-feeding after rehydration in infants with gastroenteritis. Authors concluded that the routine use of a low-lactose formula is beneficial during re-feeding after rehydration in infants with gastroenteritis [11].

In contrast to studies indicating beneficial effects of lactose-free formula for the management of acute childhood diarrhea, Brown and colleagues in a meta-analysis of 29 randomized controlled trials concluded that most of the children with acute diarrhea can be successfully managed with continued feeding of undiluted non-human milk and routine dilution of milk. This meta-analysis concluded that routine use of lactose-free formula is therefore, not necessary, especially when ORS and early feeding (in addition to milk) form the basic approach to the clinical management of diarrhea in infants and children. This analysis, however, did not address the confounding effects of severity of diarrhea, degree of malnutrition, or young age (less than 1 y) in the patients [12]. A recent comparative trial that evaluated the

effectiveness of zinc, probiotic bacteria, and lactose-free formula and their different combinations in the treatment of acute diarrhea in children found no additional value to rehydration therapy for different combination of adjunct therapies except some beneficial effects for those receiving zinc/zinc plus probiotic [13]. Although we did not find beneficial effects of lactose-free over lactose-containing formula on weight change during treatment of diarrhea, time to relief from diarrhea was significantly reduced which in turn may reduce the mortality and morbidity of acute childhood diarrhea. However, there are some limitations to our study which need to be accounted. There were baseline differences between the two groups probably because allocation was not randomized, though we did a multivariate analysis and controlled baseline differences. The follow-up was short-term; we did not determine other factors such as acidosis and plasma electrolyte level, which may indirectly be influenced by lactose-free diet while decreasing the diarrheal duration.

## Conclusion

According to the results of the present study, lactose-free, compared with the lactose-containing, formula was shown to be effective in dietary management of acute diarrhea by reducing time to diarrhea relief. Early administration of

lactose-free formula for children presenting with acute diarrhea can result in a more rapid remission of diarrhea and thus perhaps less mortality and morbidity. Further trials with longer follow-ups are warranted to evaluate long-term results such as weight change and feeding problems in this regard.

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**Conflict of Interest:** None

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