



A Study of Probiotics Use in the Acute Diarrhoea in the Infants & Children

Authors

Dr Mukesh Beniwal¹, Dr Anil Lahoti²

¹Assistant Professor, Department of Paediatrics, S.P. Medical College, Bikaner, (Rajsthan)

Email: dr.mukesh.beniwal07@gmail.com, Mobile no: 759725077

²Assistant Professor, Department of Paediatrics, S.P. Medical College, Bikaner, (Rajsthan)

Email: Lahotianil04@gmail.com, Mobile no.: 9828851550

Abstract

Background: A wide assortment of organisms cause acute diarrhoea and many of them have been discovered only in recent years such as rotavirus and campylobacter. The management of acute diarrhoea consist of the replacement of lost fluid with glucose electrolyte oral rehydration solution. Probiotics are dietary supplements containing beneficial bacteria or yeast. we planned to conduct To compare the efficacy of curd (National Probiotic) with Probiotics (LAB) available in market in term of correction of dehydration, reduction in diarrhoea duration & frequency.

Material & Methods: The present study was conducted in the Department of Paediatrics, Regional Institute for Maternal & Child Health (RIMCH) – Umaid Hospital, Dr. S. N. Medical College, Jodhpur from January 2008 to December 2008. In our study we included children aged between 3 months to 5 years admitted with some dehydration due to acute diarrhoea of duration 5 days or less. Children were randomised in to two groups i.e. Group 'A' and Group 'B'. A simple randomisation done using a computer generated random number table on a master list.

Results: In present study to observed that majority of children (84%) were below 2 year of age. The present study showed the mean age (in months) and mean weight (in Kilograms) of patients were 16.88 ± 13.24 and 7.80 ± 2.25 respectively. The mean frequency of motion and duration of diarrhoea were 8.20 ± 2.45 motions/day and 2.17 ± 1.22 days respectively. Serum levels of sodium and potassium at admission (mEq/L) were 142.72 ± 11.90 and 3.83 ± 0.55 respectively. All these parameters were comparable in between both of the groups as observed p values were non-significant.

Conclusion: Finally, our study has shown that the use of Indian Dahi or Commercially available probiotics is equally effective in the acute childhood diarrhoea as here was no statistically significant difference observed in the various outcome variables but Indian Dahi (curd) has several advantages over probiotics, such as better acceptance, easy availability at all places specially in the village and rural areas and cheaper then probiotic products.

Keywords: Probiotics, Curd, Acute Diarrhoea, Stool, Motion.

Introduction

Diarrhoea defined as the passage of 3 or more liquid or watery stools in a day. However, it is the recent change in consistency and character of

stools rather than the number of stools that is more important.⁽¹⁾

The WHO/ UNICEF defined “acute diarrhoea” as an attack of sudden onset which usually lasts for 3

to 7 days but may last up to 10-14 days. Diarrhoea is therefore a symptom and it is preferable to consider diarrhoea if there is increased frequency, volume, and fluidity of stools. It is also a sign when the loss of water (stool volume) is more than 15gm/kg/day in children <3 year and >200gm/day in children >3 year of age. (Pickering and Snyder 1996)

Comprising estimates of the current global burden of diarrhoeal disease with previously published estimates, highlights that the incidence of diarrhoea has not changed much, although overall diarrhoea mortality has declined. For children aged under 5 years in developing countries, a median of 3.2 episodes of diarrhoea occurred per child-year, which is similar to that reported previously. Estimates of mortality indicate that 4.9 children per 1000 per year died in the developing regions as a result of diarrhoeal illness in the first 5 year in 1959-1979 and 5.6 per 1000 per year in 1980-1989. The decrease is more pronounced in infants. According to recent estimates for 2000-2003 diarrhoeal disease accounts for about 17 percent of under 5 mortality in post neonatal period and 3 percent of neonatal deaths.⁽²⁾

In India diarrhoeal disease is a major health problem among children under the age of 5 years. During 2005 about 1.07 million cases of acute diarrhoea were reported in India ⁽³⁾. The actual incidence must be many folds. The National Diarrhoeal Disease Control Programme has made a significant contribution in averting deaths among children under 5 years of age. Diarrhoeal diseases cause a heavy economic burden on health services.

In developing countries diarrhoea is almost universally infectious in origin. A wide assortment of organisms cause acute diarrhoea and many of them have been discovered only in recent years such as rotavirus and campylobacter. Man is the principal reservoir.

The Indian Academy of Paediatrics National Task Force has recommended that all doctors should prescribe ORS for all ages in all type of diarrhoea, the group noted that the new improved universal

ORS recommended by the WHO containing Sodium 75 mmol/L and Glucose 75mmol/L is identified more suitable for children.⁽⁴⁾

The management of acute diarrhoea consist of the replacement of lost fluid with glucose electrolyte oral rehydration solution. This solution however reduces neither the severity nor the duration of diarrhoea.⁽⁵⁾

For at least a century, researcher have hypothesized that live bacterial cultures, such as those found in YOGURT, may helps to treat and prevent diarrhoea. (Metchnikoff).⁽⁶⁾

Yoghurt has nutritional benefits beyond those of milk: people who are moderately lactose-intolerant can enjoy yoghurt without ill effects, because the lactose in the milk precursor is converted to lactic acid by the bacterial culture. The reduction of lactose bypasses the affected individuals' need to process the milk sugar themselves.⁽⁷⁾

Yoghurt also has medical uses, in particular for a variety of gastrointestinal conditions,⁽⁸⁾ and in preventing antibiotic-associated diarrhoea. One study suggests that eating yoghurt containing *L. acidophilus* helps prevent vulvovaginal candidiasis, though the evidence is not conclusive.⁽⁹⁾

Yoghurt is believed to promote good gum health, possibly because of the probiotic effect of lactic acids present in yoghurt.⁽¹⁰⁾

Probiotics are dietary supplements containing beneficial bacteria or yeast. According to currently adopted definition by FAO/WHO probiotics are "Live Micro-organism which when administered in adequate amount confers a health benefit on the host".⁽¹¹⁾

Studies published in the world literature have concluded that *Lactobacillus* is indeed safe and effective in treating and preventing infectious diarrhoea, antibiotics diarrhoea and diarrhoea in children who are usually susceptible as a result of poor nutrition, impaired immune status and frequent exposure to pathogens. Despite these reports health professionals do not recommends *Lactobacillus*, perhaps believing that its effectiveness has not yet been approved.⁽¹²⁾

In India, study done at J. N. Medical College, AMU Aligarh (Department of Paediatrics) showed that is no significant benefit of tyndalized *Lactobacillus acidophilus* (Probiotics) in acute diarrhoea in infants & children, Another study conducted at Department of Paediatrics, J.S.S. Medical College, Hospital Mysore showed that probiotics have better efficacy than placebo in the management of acute diarrhoea. Keeping the above hypothesis/ study in mind we planned to conduct To compare the efficacy of curd (National Probiotic) with Probiotics (LAB) available in market in term of correction of dehydration, reduction in diarrhoea duration & frequency.

Material & Methods

The present study was conducted in the Department of Paediatrics, Regional Institute for Maternal & Child Health (RIMCH) – Unaid Hospital, Dr. S. N. Medical College, Jodhpur from January 2008 to December 2008.

In our study we included children aged between 3 months to 5 years admitted with some dehydration due to acute diarrhoea of duration 5 days or less. If child was in severe dehydration at the time of admission, he/she was not included in our study because these children required intravenous fluids for management and in the same way children with no dehydration were also not included in our study as they do not required hospitalization for management. The degree of dehydration was assessed in every case as per guidelines laid down by WHO.

The patients with septicaemia, paralytic ileus, malnutrition grade III and IV (graded on the basis of present weight as per IAP classification) and those having significant systemic illness were excluded from the study. Thus we selected total 100 children who were eligible for our study.

The eligible children were allotted a study number. These numbers corresponded to the order of patients entering in the trial. Children were randomised in to two groups i.e. Group 'A' and Group 'B'. A simple randomisation done using a

computer generated random number table on a master list.

In our study we used low Osmolarity ORS (ORS-224; marketed by CURATUO Health Care Pvt. Ltd.) with total Osmolarity – 224 mmol/litre, Glucose-84mmol/litre, Sodium-60mmol/litre, Citrate-10 mmol/litre, Potassium-20mmol/litre (approximately) for both study groups. It was followed by maintenance ORS at a rate of 10-20 ml/kg body weight for each loose stool.

Group A (50 children) – were put on low Osmolarity ORS with usual diet and Indian Dahi (natural Probiotic). Indian Dahi (curd) was offered ad libum (at least 15gm/kg body weight of patient per day for 3 days). Indian Dahi (Lf 40) containing 10(8) of each *Lactococcus lactis*, *Lactococcus lactis cremoris* and *Leuconostoc mesenteroides cremoris* per gram.

Group B (50 children) – were put on low Osmolarity ORS with usual diet and market available Probiotic (SPORLAC sachets' Manufactured in India by UNI-SNAKYO LTD.). In Probiotics *lactis acid bacillus* (Earlier known as *Lactobacillus sporogenes*) spores were used in dose of 1.35×10^9 spores per patient and given thrice a day for three days (1 sachet of 1gm powder contain not less than 150 million spores of lactic acid bacillus).

A detailed history regarding epidemiological profile included residential status, source of water supply, type of house, family size, educational status of parents, type of feeding, socio-economic status (Per capita income) and history of present diarrhoeal episode (included duration, frequency, volume, consistency and colour of stool with associated vomiting and other complaints) was taken at the time of admission and recorded on pretested Performa specially designed for this study.

If the patients of study group did not improve & needed IV fluids then these patients were excluded from study and considered as treatment failure.

Blood samples (venous blood) were drawn with all aseptic precautions and a free flow of blood

droplets was maintained. Blood samples (2ml) for blood urea, serum creatinine and serum electrolytes was collected in a dry, clean test tube, subjected to laboratory attached to our department. Blood for hemogram was collected in EDTA vial (1ml) and analysed in the central laboratory attached to the Umaid Hospital, Jodhpur.

The serum electrolytes were performed by using 'Flame photometry' method as described by Harold Varley; the blood urea was done by using SEAC Computerised Photo analyser S-267 (manufactured by Ames Division of MILES India Ltd.), while the hemogram was done by using Haemocamp auto analyser (manufactured by MILES India Ltd.).

For measuring stool volume in the cases of older children we collected the motion in a disposable container (cup or plastic glass) & for younger we first took weight of dry napkin or diaper, then the same diaper or napkin weighted with motion and subtracted dry napkin's weight from wet napkin's weight. Mother's were also educated/trained to collect urine in container or bottle, for infants we used minicombs to collect the urine for measuring urine output.

Patients were discharged 24 hour after cessation of diarrhoea (passage of formed stool or passage of no stool for 12 consecutive hours) or at the end of five days from admission.

At the time of discharge each patient was categorized as having completed the trial, treatment failure (not improved or needed intravenous fluids) or as withdrawal (left the study in between/ absconded). The data thus collected were analysed statistically.

Data was analysed with the help of SPSS version 10. Continuous data were compared by student 't' test. The chi-squared test or Fischer's exact test was used to test the difference between groups. Statistical significance was set at $P = 0.05$.

Results

In present study to observed that majority of children (84%) were below 2 year of age. Most of

these were between 3 months to one year of age (55%). 23% children were aged less than 6 months (table 1).

The present study showed the mean age (in months) and mean weight (in Kilograms) of patients were 16.88 ± 13.24 and 7.80 ± 2.25 respectively. The mean frequency of motion and duration of diarrhoea were 8.20 ± 2.45 motions/day and 2.17 ± 1.22 days respectively. Serum levels of sodium and potassium at admission (mEq/L) were 142.72 ± 11.90 and 3.83 ± 0.55 respectively. All these parameters were comparable in between both of the groups as observed p values were non-significant (table 2). The time of appearance of first semi formed stool was 50.64 ± 13.40 hours for group A and 46.70 ± 14.40 hours for group B with p value of >0.2 . Thus there was no significant difference duration of diarrhoea between the two groups (table 3).

If we see the difference between other variable such as weight gain and ORS consumed in first 6 hours, we again observed that there is no statistically significant difference. With the time the mean numbers of stools were decreasing in both the groups with a larger decreased in group B. In the group A the mean number of stools decreased from 8.36 ± 2.48 per 24 hours at admission to 7.22 ± 2.63 in first 24 hours, to 3.83 ± 1.66 in the next 24 hours to 1.95 ± 1.21 by the end of 72 hours where as the mean stools number per 24 hour in group B at same time periods were 8.04 ± 2.43 , 6.29 ± 1.94 , 2.93 ± 1.25 and 1.80 ± 1.07 respectively. The difference in the numbers of stools being passed at the end of 72 hours had p value >0.5 , which again was statistically insignificant (table 3).

Table I: Distribution of cases according to age and sex

Age group (months)	Group A			Group B			Total (A+B)
	Male	Female	Total	Male	Female	Total	
3 to \leq 6	9(18)	4(8)	13(26)	6(12)	4(8)	10(20)	23(23)
6-12	15(30)	3(6)	18(36)	18(36)	2(8)	14(28)	32(32)
12-24	5(10)	7(14)	12(24)	10(20)	7(14)	17(34)	29(29)
25-36	2(4)	1(2)	3(6)	2(4)	2(4)	4(8)	7(7)
37-48	2(4)	1(2)	3(6)	1(2)	2(4)	3(6)	6(6)
49-60	1(2)	-	1(2)	1(2)	1(2)	2(4)	3(3)
Total	34(68)	16(32)	50(100)	32(64)	18(36)	50(100)	100(100)

Table-II: Distribution of cases according to various admission characteristics

Characteristics	Group A Mean \pm S.D.	Group B Mean \pm S.D.	P Value	Total Mean \pm S.D.
Weight in kg	7.62 \pm 2.32	7.93 \pm 2.20	>0.6	7.80 \pm 2.25
Age in months	14.7 \pm 12.20	18.5 \pm 13.98	>0.1	16.88 \pm 13.24
Frequency of motion (per 24 hours)	8.36 \pm 2.48	8.04 \pm 2.43	>0.5	8.20 \pm 2.45
Duration of diarrhoea in days	2.08 \pm 1.29	2.27 \pm 1.17	>0.5	2.17 \pm 1.22
Sodium level in mEq/L	142.68 \pm 11.80	142.76 \pm 11.95	>0.9	142.72 \pm 11.90
Potassium level in mEq/L	\pm 0.53	3.85 \pm 0.58	>0.7	3.83 \pm 0.55

Table-III: Comparison of end parameters between group A and group B

Characteristics	Group A (n= 48) (Mean \pm S.D.)	Group B (n= 48) (Mean \pm S.D.)	P value	
Time of appearance of first semi formed stool (in hours)	50.64 \pm 13.40	46.70 \pm 14.40	>0.2	
Number of Stools	0-6 hours	1.77 \pm 1.13	1.65 \pm 0.84	>0.6
	0-24 hours	7.22 \pm 2.63	6.29 \pm 1.94	>0.1
	25-48 hours	3.83 \pm 1.66	2.93 \pm 1.25	<0.01
	49-72 hours	1.95 \pm 1.21	1.80 \pm 1.07	>0.5
Stool weight (in grams)	0-6 hours	46.14 \pm 44.83	46.06 \pm 30.62	>0.9
	0-24 hours	167.53 \pm 109.58	155.74 \pm 74.27	>0.5
	25-48 hours	81.56 \pm 71.60	68.19 \pm 41.31	>0.3
	49-72 hours	40.74 \pm 2.54	42.17 \pm 28.43	>0.8
ORS consumed in first 6 hr (in ml)	568.75 \pm 166.60	605.31 \pm 175.15	>0.3	
Weight gain in grams	121.94 \pm 94.21	113.29 \pm 73.85	>0.7	

Discussion

Diarrhoeal diseases rank with acute respiratory infections as among the major causes of morbidity and mortality among children under 5 years of age. The World Health Organization started the Diarrhoeal Disease Control Programme (DDCP) in 1980 with the objective to decrease diarrhoeal mortality and morbidity among young children in developing countries. Despite improving trends in mortality rates, there was no concurrent decrease in morbidity rates attributed to diarrhoea. Persistent high rates of morbidity are of concern because early childhood diarrhoea may have long-term effects on linear growth and physical and cognitive function.

Though oral rehydration therapy is the corner stone of programmes for control of diarrhoeal diseases and the IAP National task Force has recommended that all doctors should prescribe ORS for all ages in all types of diarrhoea, a search has continued for an agent that could prove to be safe and efficacious in reducing the duration of diarrhoeal episode. In recent years it has shown that probiotics can promote a more rapid recovery of acute diarrhoea. For at least a century, researcher have hypothesized that live bacterial cultures, such as those found in YOGHURT, may helps to treat and prevent diarrhoea. (Metchnikoff)⁽⁶⁾. According to current scientific concepts, yoghurt cultures are probiotics if a beneficial

physiological effect can be obtained by consumption of the live cultures and the benefit has been substantiated appropriately in human studies. Till date so many studies conducted to evaluate the roll of probiotics and yoghurt use in acute diarrhoea separately, in majority of these studies it was shown that probiotics and yoghurt (curd) both were effective to prevent and treat acute childhood diarrhoea.

To the best of our knowledge no study in India has been done to compare the efficacy of probiotics and curd to treat the diarrhoea. As we know that curd is easily available and cheaper than probiotics preparation and in addition it has nutritive value. So our study planned with the above objective kept in mind.

In our study 84% cases were below 2 year of age. Most of these between 3 months to one year of age i.e. 55% of study population. Only 16% children were aged more then 2 year. This age distribution is similar to that reported by Shrivastava et al.⁽¹³⁾, Naruka et al⁽¹⁴⁾ and Ghai et al⁽¹⁵⁾, they observed diarrhoea in 81%, 73% and 92% cases below 2 year of age.

The high incidence of diarrhoea in males (66%) as compared to females (34%) may be due to general preponderance of male sex seen in hospitalized patients from various causes. Such preponderance has also been reported by earlier workers like Ghai and Kalra⁽¹⁵⁾, Shrivastvs and Bhatnagar⁽¹⁶⁾ and Jain MK et al.⁽¹⁷⁾.

More than half of the children (53%) had 7-10 loose motions per day at the time of admission and vomiting was associated with 79% cases. Naruka et al.⁽¹⁴⁾ and Gupta BD et al (1994)⁽¹⁸⁾ also observed the similar finding.

In our study 60% children had malnutrition (PEM) grade I or II. (As the cases with PEM grade III and IV were not included in our study, so that over all association of malnutrition with diarrhoea must be more then we observed). Our findings are similar to as observed by Ghai and Jaiswal⁽¹⁹⁾ and Srivastva et al.⁽¹⁶⁾

Treatment failure rate of our study groups (4%) were similar to those observed by earlier worker.

Boudraa et al 2001 with yoghurt use⁽²⁰⁾, Jobst Henker et al 2005 with yoghurt use⁽²¹⁾, Enduaro Salazar et al with probiotics use⁽²²⁾ and Khanna et al 2005 with probiotics use⁽²³⁾ observed failure rate of 3.6%,5.5%,21% and 2.5% respectively.

Pashapour et al 2005⁽²⁴⁾ observed the mean duration of diarrhoea was 2.7 ± 0.91 days in yoghurt treated group. Agarwal K. N et al 2001⁽²⁵⁾ used Indian Dahi to treat diarrhoea in a hospital study. Indian Dahi administration reduced mean duration of diarrhoea by 0.3 day and they conclude that Indian Dahi can significantly reduce the duration of diarrhoea in children.

Isolaruri et al 1994⁽²⁶⁾ observed that the mean duration of diarrhoea was significantly lower in probiotics treated group (1.4 day) compared to yoghurt treated group (2.4 days). While with use of probiotics Billoo et al 2000⁽²⁷⁾, Jobst Henker et al⁽²¹⁾, Enduaro et al⁽²²⁾ Roberto Berni Canani et al⁽²⁸⁾ and Khanna et al 2000⁽²³⁾ observed that the mean duration of diarrhoea was 3.6 days, 2.5 days, 58.5 hours, 78.5 hours and 58.78 hours respectively. Similarly Szajewska H. et al 2006;⁽²⁹⁾ observed that probiotics use were significantly reduced the duration of diarrhoea.

Pashapour et al 2005⁽²⁴⁾ observed the mean frequencies at day third were 4.3 ± 1.74 days in yoghurt treated group. Van Neil et al⁽³⁰⁾ and Billoo et al 2000⁽²⁷⁾ observed that in probiotics treated groups frequencies at day third were 1.6 and 2.7 respectively.

Conclusion

In conclusion we observed that the children aged less than 2 year are more vulnerable for acute diarrhoeal illness. Barest-fed babies seem to suffer less frequently with diarrhoea, and hence prolongation of breast feeding may be protective to the baby. Finally, our study has shown that the use of Indian Dahi or Commercially available probiotics is equally effective in the acute childhood diarrhoea as here was no statistically significant difference observed in the various outcome variables but Indian Dahi (curd) has several advantages over probiotics, such as better

acceptance, easy availability at all places specially in the village and rural areas and cheaper than probiotic products. In addition to those advantages it is a part of Indian ancestral diet and has nutritive value: since most of our children with diarrhoea are already malnourished and Indian dahi can be easily mixed with rice or khichri, which make this diet more palatable and nutritive too. So by this study we recommend universal use of Indian Dahi (curd/yoghurt) in acute childhood diarrhoea.

References

1. WHO, a manual for the treatment of diarrhoea, Programme for control of diarrhoea diseases. WHO/COD/SER/80.2. Rev. 2.1990.
2. Park's text book of preventive and social medicine; 19th edition. 183-188.
3. Govt. of India (2006), Health information of India, Ministry of Health and Family welfare, New Delhi.
4. Recommendation of the IAP, National Task for use of ORS in diarrhoea, Aug.2003/2006. Indian pediatrics 2007,vol-44;380-389.
5. Alam NH, Ashraf H; Treatment of infectious diarrhoea in children, Paediatr Drugs2003; 05: 151-65/Medline.
6. Metchnikoff E Sur al flore du Corps humain, Manchester Lit Philos Soc,1901;45:1-38.
7. J.C. Kolars et al., Yoghurt-an auto digesting source of lactose. New England Journal of Medicine, 310:1-3 (1984).
8. O. Adolfsson et al., "Yoghurt and gut function", American Journal of Clinical Nutrition 80:2:245-256(2004)
9. Ripudaman S. Beniwal, et al., "A Randomized Trial of Yoghurt for Prevention of Antibiotic-Associated diarrhoea", Digestive Diseases and Science 48:10:2077-2082 (October,2003) doi:10.1023/A:1023155328638
10. Erika N. Ringdahl, "Treatment of Recurrent Vulvovaginal Candidiasis", American Family Physician 61:11 (June 1,2000)
11. FAO/WHO(2001); Health Nutritional Properties of Probiotics
12. Lewis SJ, Freedman AR, Review article; The use of bio therapeutic agent in the prevention and treatment of gastrointestinal diseases ; 1998;12:807-822/ Medline.
13. Shrivastava JR, Verma V, Garg Bk. Acute diarrhoea in childhood : a clinicobacteriological study at Kanpur. Indian J Pediatr1968; 35:214-217
14. Naruka B, Sharma U, Saxena S. A clinical profile of acute diarrhoea in infancy and childhood. Indian J Pediatr1974;41:374.
15. Ghai OP, Kalra SL, Jaiswal VN. Epidemiology of diarrhoea in infants and preschool children in a rural community near Delhi. Indian Pediatr; 6:263.
16. Shrivastavs AK, Bhatnagar JK, Prasad BS, Sharma NL. A clinicoepidemiological study of diarrhoea in hospitalized children at Lucknow. Indian J Pediatr Med Res 1973; 61: 96.
17. Jain Mk et al. Evaluation of clinical criteria for the management of acute diarrhoea in infants and children. Indian Pediatr 1983; 20: 489-498.
18. Gupta BD, Singh J. A study of standard WHO-ORS versus plain water with usual diet in the management of acute diarrhoea dehydration. A dissertation submitted to University of Rajasthan for the degree of MD paediatrics, 1994.
19. Ghai OP, Jaiswal VN. Relationship of undernutrition to diarrhoea in infants and children. Indian J Med Res 1970; 58:789.
20. Boudraa G, Benbouabdellah M, Hachelaf W, Boisset M, Desjeux JF & Touhami M. (2001) Effect of feeding yoghurt versus milk in children with acute diarrhoea and carbohydrate malabsorption. J Pediatr Gastroenterol Nutr 33, 307-313.

21. Jobst Henker, Martin Laass, Boris M. Blokhin, Yuriy K. Bolbot, Vitaliy G. Maydannik, Martina Elze, Corinna Wolff, And Jurgen Schulze The Probiotics Escherichia coli strain Nissle 1917 (EcN) stops acute diarrhoea in infants and toddlers Eur J Pediatr. 2007 April; 166(4): 311-318
22. Eduardo Salazar-Lindo, Percy Miranda-Langschwager, Miguel Campos Sanchez, Elsa Chea-Wool and R Bradley Sack; Lactobacillus casei strain GG in the treatment of infants with acute watery diarrhoea: A randomized, double-blind, placebo controlled clinical trial; BMJ Pediatr 2004, 4:18.
23. Khanna V, Alam S, Malik A, efficacy of tyndalized Lactobacillus acidophilus in acute diarrhoea. Indian J Pediatr 2005; 935-938.
24. Pashapour N, Iou SG. Evaluation of yoghurt effect on acute diarrhoea in 6-24 month old hospitalized infants. Turk J Pediatr 2006; 48: 115-118
25. Agarwal KN, Bhasin SK et al. Feasibility studies to control acute diarrhoea in children by feeding fermented milk preparations Actimel and Indian Dahi. Eur J Clin Nutr. 2002 Dec;56 Suppl 4:S56-9
26. Isolauri, E., Kaila, M., Mykkanen, H., Ling, W.H., Salminen, S. Oral bacteriotherapy for viral gastroenteritis. Dig Dis Sci 1994, 39: 2595-600.
27. Billo AG, Memon MA, Khaskheli SA, Murtaza G, Iqbal K, Saeed Shekhani M, Siddiqi AQ. Role of a probiotic (Saccharomyces boulardii) in management and prevention of diarrhoea. World J Gastroenterol 2006; 12(28): 4557-4560
28. Roberto Berni Canani, Pia Cirillo, Gianluca Terrin, Luisa Cesarano, Maris Immacolata Spagnuolo, Anna De Vincenzo, Fabio Albano, Annalisa Passariello, Giulio De Marco, Francesco Manguso, Alfrdo Guarino, Probiotics for treatment of acute diarrhoea in children: randomised clinical trial of five different preparations; BMJ,doi:10.1136/bmj.39272.581736.55 (published 9 August 2007)
29. Szajewska H., Skorka A., Dylag M.; Meta-analysis : Saccharomyces Boulardii for treating diarrhoea in children: [http://www.medscape.com/viewarticle/552627\(2007\)](http://www.medscape.com/viewarticle/552627(2007)).
30. Van Niel, C.w., Feudtner, C., Garrison, M.M., Christakis, D.A. Lactobacillus therapy for acuteinfectious diarrhoea in children: A metaanalysis. Pediatrics 2002, 109: 678-84.