IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 17, Issue 3 Ver.8 March. (2018), PP35-40
www.iosrjournals.org

To Study The Role Of Saccharomyces Boulardii In Treatment Of Acute Watery Diarrhea In Children Aged 6 Months To 5years: Prospective Randomized Control Study.

Dr. Arvind Kumar M.D. Paeds (Specialist,Bgh) , Dr Dilip Kumar (Rims), Dr Daravat Rajkumar (Dnb, Bgh)

RATIONALE**:** To treat the diarrhoea cases by giving *saccharomyces boulardii.*

Corresponding author: Dr. Arvind Kumar M.D. Paeds (Specialist,Bgh)

***AIM** : To study the role of Saccharomyces boulardii in treatment of acute watery diarrhoea in children aged 6months to 5 years*
***OBJECTIVE**: To compare the duration of diarrhea and frequency of stools in case and control groups .*
***SETTING:** Study will be conducted in tertiary care hospital.*
***STUDY DESIGN**: prospective single blinded randomized controlled study.*
***TIME FRAME** : Study will be conducted from October 2016 to January 2018.*
***POPULATION:** Children of both sexes aged 6 months to 5 years admitted to paediatric ward of Bokaro General Hospital with acute watery diarorhea were studied.*
***SAMPLE SIZE**: A total of 100 infants and children aged between 6 months to 5 years were Included in the present study and are further divided into 2 groups of 50 each.*
***METHODS**: Children in the study arm will receive S. boulardii 250 mg orally twice a day for 3 days. Frequency and consistency of stool will be recorded after 24, 48, 72, 96, and 120 hours in both groups. Serum electrolytes will be done on admission and after 72 hours of therapy in both groups.*
***OUTCOME MEASURES**: Resolution of diarrhea will be considered when stool frequency was ≤ 2 per day*
***Primary outcome variable**s: Duration of diarrhea, Frequency of loose stools.*

Date of Submission: 01-03-2018 Date of acceptance: 19-03-2018

I. Introduction

As per WHO, diarrhoea is defined as passage of three or more loose stools per day, or more frequently than normal for an individual[1].

In the 1980s, five million children worldwide died every year because of diarrhoea, essentially because there was no readily available treatment. In the intervening 30 years, improved management of diarrhoea, such as treatment with oral rehydration solutions, intravenous fluids and zinc, has led to a substantial reduction in mortality to approximately 614 000 deaths every year. Diarrhoea is the second most common cause for the under 5 mortality[2].

According to Walker CL et al[3], diarrhoea was responsible for approximately 1.8 million deaths among children under 5 years of age in low and middle income countries[3].

Childhood diarrhoea is one of the leading causes of morbidity and mortality throughout the world, accounting for an estimated 9.9% of the 7.6 million deaths among children <5 years of age in 2010. Children in developing countries are the worst affected[4].

In India, common illness in children less than 3 years of age are fever (27%) acute respiratory infection (17%), diarrhoea (13%) and malnutrition and these are often in combination. About 2 million episodes of diarrhoea occur each year in India. Of the 6.6 million deaths among children aged 28 days to 5 year; deaths from diarrhoea are estimated to account for 1.87million. An average Indian child less than 5 years of age will have 2–3 episodes of diarrhoea[5]. Prevention of all-cases of diarrhoea; rotavirus vaccines are efficacious to prevent diarrhea specific to rotavirus. Proper hand washing, exclusive breast feeding and use water treatment are effective strategies for prevention of all causes diarrhea[6]. Oral Rehydration Therapy (ORT), a simple, cost-effective treatment given at home using either packets of Oral Rehydration Salts (ORS) or a simple home solution of sugar, salt and water can prevent about 90% of child deaths from diarrhoeal dehydration. WHO, UNICEF and its partners have helped more than 45 countries to achieve treating 80% of child diarrhoea cases with ORS[7]. Intravenous fluids are required in treatment failures associated with high frequency of stools, uncontrolled vomiting or poor oral intake due to associated infection[8]. Probiotic products have special microorganisms like bacteria or yeast in them. These are believed to reach the bowel, where they help fight the germs causing the diarrhea. The best known examples of probiotics are lactic acid bacteria in yogurts and other dairy products, as well as in certain dietary supplements. The most commonly tested probiotics were Lactobacillus casei, Saccharomyces boulardii and Enterococcus bacteria[9]. These can modify intestinal microbiota By secreting anti microbial compounds like bacteriocins, induction of producing anti microbial compounds like defensins by the host, reducing luminal pH, preventing bacterial adhesion and evasion of epithelial cells, and competition for nutrients[10].

II. Review Of Literature

WHO defines diarrhoea as, passage of ≥3 loose or watery stools/day. The term loose stool is defined as the one which takes the shape of the container. Recent change in consistency of stools is more important than number of stools[11].

Diarrhoeal diseases can be classified according to their clinical pattern as:

(i) acute watery diarrhea (i.e. diarrhea without blood lasting less than 14 days);

(ii) persistent diarrhea (i.e. diarrhea lasting 14 days or more); or

(iii) Acute bloody diarrhea (i.e. diarrhea with blood lasting less than 14 days).

Most episodes of diarrhoea in developing countries are infectious in origin. Acute diarrhoea may be watery (where features of dehydration are prominent) or dysenteric (where stools contain blood and mucus) [12].

The causes of acute diarrhea in children vary with the location, time of year, and population studied[13].

Etiological agents:

Diarrhoea is a common symptom of gastrointestinal infections caused by a wide range of pathogens, including bacteria, viruses and protozoa. Cryptosporidium have been the most frequently isolated protozoan pathogen among children seen at health facilities and is frequently found among HIV-positive patients[1].

A study conducted by Houque SS et al, showed that, Rotavirus was most frequently detected in children between 6 and 11 months old. Other agents which were Escherichia coli, Vibrio cholerae, Shigella and Salmonella[14]. Indiscriminate stool disposal by the mothers, lack of hand-washing before feeding their children and hand-washing without soap were associated with increased risk as studied by Lakshminarayanan et al[15]. Among the above mentioned risk factors, breastfeeding may be the most important modifiable risk factor for reducing duration of diarrhea[16].

Pathophysiology:

Viral and protozoan pathogens act through different mechanisms to induce secretory diarrhea. Rotaviruses, noroviruses and protozoa such as *Cryptosporidium* primarily infect and damage the absorptive villous tips, leaving secretory crypts unbalanced, to cause net secretion and diarrhea. Cholera, the prototype of secretory diarrhea, is caused by the enterotoxin of *Vibrio cholerae* (cholera toxin) [17].

Clinical presentation and complications:

The main clinical features observed in a case of acute episode of diarrhoea are vomiting, nausea, pain abdomen, dehydration, metabolic acidosis, fever, impaired consciousness, convulsions, circulatory failure, shock, pre renal azotemia[18].

Management:

The WHO has set the following therapeutic goals for the treatment of acute diarrhoea

1. to prevent dehydration,
2. to treat dehydration,
3. to prevent nutritional damage,
4. To reduce the duration and severity of diarrhoea and the occurrence of future episodes[19].

III. Oral Rehydration Therapy

Dr Nobert Hirschhom, who played a major role in the development of ORT, agrees with Greenough, but gives more credit to Darrow for having pinpointed which electrolytes needed replenishing. Finally ORT developed in the late 1960 by researchers in India and Bangladesh for treatment of cholera[20].

Role of Zn in Acute watery diarrhoea:

The positive action by zinc in acute watery diarrhoea derives from a regulation of intestinal fluid transport, mucosal integrity, immunity, gene expression, and oxidative stress[21]. It acts as a K channel blocker of adenosine 3', 5'-cyclic monophosphate-mediated chlorine secretion[22].

Role of Probiotics in acute watery diarrhoea:
Probiotics have been defined by the joint FAO/WHO Working Group (Food and Agriculture Organisation/World Health Organisation) as "live microorganisms that when administered in adequate amount confer a health benefit on the host".
S. boulardii is a tropical strain of yeast first isolated from Lychee and Mangosteen fruit in 1923 by a French scientist Henri Boulard[23].
S. boulardii survives best at 37°C[24]; it is generally administered in lyophilized powder.
Probiotics have been shown to be safe in immunocompetent hosts in an outpatient setting. However, administration of probiotics to immunocompromised, chronically ill, hospitalized patients with GI disorders, and indwelling catheters may predispose them to probiotic sepsis[25].
The recommended dose of S. boulardii in children over 2 months of age is 250 mg given twice daily. It is recommended that it not be used in children under 2 months of age without the supervision of a health care provider. The usual adult dose is 500 mg (2 sachets) once daily for the prevention of diarrhoea or twice daily for treatment. Treatment duration typically ranges from 1 to 4 weeks for acute or antibiotic-associated diarrhea[26].

Studies on Saccharomyces:
In a study done by Kurugöl Z, Koturoğlu G[27] in 2005, it was found that medians of the average stool frequency after the second day of the treatment were significantly lower in the S. boulardii group than in the placebo group.
Similar findings were found by Htwe K, Yee KS, Tin M, Vandenplas Y et al during their randomised study in Myanmar children[28].
A double blind randomised controlled trial conducted by Riaz M, Alam S, Malik A, Ali SM et al found that early change in stool consistency to semi formed stools with S. Boulardii administration along with the standard therapy[29].
A systematic review and meta-analysis conducted by Dinleyici EC, Eren M, Ozen M, Yargic ZA, VandenplasY et al found the benifits of S. boulardii in decrease in hospital stay and duration of diarrhea in developing countries[30].
Burande Meeta A, Burande Amit R[31], studied the efficacy of Saccharomyces boulardii strain in treatment of acute diarrhoea in Indian children, by prospective, parallel; single blind randomized controlled clinical trial in 2013.

In another meta-analysis conducted by Feizizadeh S, Salehi-Abargouei A, Akbari V[32], in 2014 to see the efficacy of Saccharomyces boulardii for treatment of acute childhood diarrhoea, both the above studies found significance reduction in duration of diarrhoea when S boulardii co administration with standard diarrheal therapy .

IV. Aims And Objectives

Aim-
To study the role of Saccharomyces boulardii in treatment of acute watery diarrhoea in children aged 6months to 5 years

Objectives:
1. To compare the duration of diarrhea in case and control groups.
2. To compare the frequency of stools in case and control groups.

V. Material And Methods

Setting area: Paediatric ward, Bokaro General Hospital, Bokaro steel city,Jharkhand.

Study design and period: This is a prospective single blinded randomized controlled study is proposed to be carried out between October 2016 to January 2018 among children aged 6 months to 5 yrs.

Study population: Children of both sexes aged 6 months to 5 years admitted to paediatric ward of Bokaro General Hospital with acute watery diarrhea were studied.

Sample technique: Every alternate child was enrolled in group-I and Group-II as per inclusion and exclusion criteria and after taking informed consent.
Group-I: children treated with Saccharomyces boulardii for 3 days + new WHO ORS.
Group-II: children treated with only new WHO ORS

Inclusion Criteria: -
1. Acute watery diarrhea less than 7 days duration
2. Children aged 6 months to 5 years.
3. Sex: Both Males and Females.

Data collection technique:
1. Acute watery diarrhea will be diagnosed as per WHO definition[1].
2. A detailed history and clinical examination will be recorded on pre-defined proforma.

All children will be weighed and measurements will be converted into weight for age, percentage of standard for each child using NCHS standards.
Based on dehydration status children will be treated for severity of dehydration as per WHO guidelines 2006.
They will be randomly divided into two groups (group-I & group-II). Principles of single blinded randomized controlled trial will be followed in both groups.
1. Group-I patients will be treated with 250 mg sachets of S. boulardii (SB) twice a day per oral for 3 days along with new WHO ORS and IV fluids when indicated.
2. Group-II patients will be treated with only new WHO ORS & IV fluids wherever indicated.

Dosage and administration of S. boulardii (SB):

Children in the study arm will receive S. boulardii 250 mg orally twice a day for 3 days as lyophilized powder in a sachet weighing 282.5 mg equivalent to 250 mg of yeast. S. boulardii used in the study will be "ECONORM" manufactured by Dr. Reddy's lab. Antibiotics, antisecretory, other drugs will not prescribed in both groups. Patients of both groups will receive cereal based diet for acute diarrhea as prescribed by dietician in our hospital.

Frequency and consistency of stool will be recorded after 24, 48, 72, 96, and 120 hours in both groups. Frequency recorded as tally marking and consistency will also be recorded as watery, semisolid and solid stool.

Serum electrolytes will be done on admission and after 72 hours of therapy in both groups so as to observe any effect of the drug. Resolution of diarrhea will be considered when stool frequency was ≤ 2 per day

Primary outcome variables
1. Duration of diarrhea
2. Frequency of loose stools.

VI. Observations

Stool frequency on admission among the Group I and Group II (block 1)

	Group I		Group II		t-statistic	P Value
	n	Mean ± SD	n	Mean ± SD		
Frequency of stool on admission	25	12.08 ± 3.58	25	11.6 ± 3.12	0.505	0.615

Stool frequency on admission among the Group-III and Group-IV (block2)

	Group III		Group IV		t-statistic	P Value
	N	Mean ± SD	n	Mean ± SD		
Frequency of stool on admission	25	10.52± 1.71	25	11.16 ± 2.13	1.169	0.247

Comparison of mean duration of diarrhea in Group I and Group II (block 1)

	Group I		Group II		P Value
	Mean ± SD	Median (Min - Max)	Mean ± SD	Median (Min - Max)	
Duration of diarrhea (hrs)	76.32 ± 24.2	72(48 - 120)	95.52 ± 25.09	96 (48 - 120)	0.011

Comparison of mean duration of diarrhea in Group-III and Group IV(block 2)

	Group III		Group IV		P Value
	Mean ± SD	Median (Min - Max)	Mean ± SD	Median (Min - Max)	
Duration of diarrhea (hrs)	77.28 ± 26.17	72(48 - 120)	97.92 ± 25.8	96 (48 - 120)	0.011

Observational Findings In Present Study:

- There was statistically significant difference in resolution of diarrhea between the four groups. In block 1 at the end of 3 days, 28% of children in Group-I improved as compared to 16% in Group-II. Also on day 5, 88% of children in group-I showed resolution of diarrhea as compared to 64 % in group-II.
- In block 2 at the end of 3 days, 32% of children in Group- III improved as compared to 16% in group-IV. Also on day 5, 80% of children in Group- II showed resolution of diarrhea as compared to 64 % in group-IV.
- Therefore children receiving S. boulardii along with ORS improved significantly earlier than those children who received ORS only.
- There were statistically Significant differences in four groups according to their mean frequency of stool on day 2, day 3, day 4, and day 5. In this study, patients treated with saccharomyces boulardii with ORS had fewer stool than patients treated with only ORS. Therefore, saccharomyces boulardii significantly decreased the frequency of stool in acute diarrhea.

References

[1]. Wardlaw T, Salama P, Brocklehurst C, Chopra M, Mason E.Diarrhoea: why children are still dying and what can be done. Lancet. 2010 Mar 13;375(9718):870-2. doi: 10.1016/S0140-6736(09)61798-0. Epub 2009 Oct 14.

[2]. Rahman AE, Moinuddin M, Molla M, Worku A, Hurt L, Kirkwood B. Et al. Childhood diarrhoeal deaths in seven low- and middle -income countries. Bull World Health Organ. 2014 Sep 1;92(9):664-71. doi: 10.2471/BLT.13.134809. Epub 2014 Jun 23.

[3]. Walker CL[1], Aryee MJ, Boschi-Pinto C, Black RE. Estimating diarrhea mortality among young children in low and middle income countries. . PLoS One. 2012;7(1):e29151. doi: 10.1371/journal.pone.0029151. Epub 2012 Jan 3.

[4]. Sarkar R, Tate JE, Ajjampur SS, Kattula D, John J, Ward HD.Et al. Burden of diarrhea, hospitalization and mortality due to cryptosporidial infections in Indian children. PLoS Negl Trop Dis. 2014 Jul 24;8(7):e3042. doi: 10.1371/journal.pntd.0003042. eCollection 2014.

[5]. Avachat SS, Phalke VD, Phalke DB, Aarif SM, Kalakoti P. A cross

[6]. sectional study of sociodemographic determinants of recurrent diarrhoea among children under five ofrural area of Western Mahara shtra, India. Australas Med J. 2011;4(2):72-5. doi: 10.4066/AMJ.2011.524. Epub 2011 Feb 28.

[7]. Shah D, Choudhury P, Gupta P, Mathew JL, Gera T, Gogia S. Et al., Promoting appropriate management of diarrhea: a systematic review of literature for advocacy and action: UNICEF-PHFI series on newborn and child health, India. Indian Pediatr. 2012 Aug;49(8):627-49.

[8]. ORT now helps save more than 1 million children's lives each year. Available from: http://rehydrate. Org/ ors/index.httm# 1million

[9]. Bhan MK. Current concepts in management of acute diarrhea. Indian Pediatr. 2003 May;40(5):463-76.

[10]. Faure C. Role of antidiarrhoeal drugs as adjunctive therapies for acute diarrhoea in children. Int J Pediatr. 2013;2013:612403. doi: 10.1155/2013/612403. Epub 2013 Mar 3.

[11]. Gerritsen J, Smidt H, Rijkers G T, and de Vos W M,Intestinal microbiota in human health and disease: the impact of probiotics.Genes Nutr. 2011 Aug; 6(3): 209–240.Published online 2011 May 27. doi: 10.1007/s12263-011-0229-7 PMCID: PMC3145058

[12]. Burgmann K, Schoepfer A. [Acute diarrhea]. Ther Umsch. 2014 Sep;71(9):529-35. doi: 10.1024/0040-5930/a000548.

[13]. Alam NH, Ashraf H. Treatment of infectious diarrhea in children. Paediatr Drugs. 2003;5(3):151-65.

[14]. Dennehy PH. Acute diarrheal disease in children: epidemiology, prevention, and treatment. Infect Dis Clin North Am. 2005 Sep;19(3):585-602

[15]. Hoque SS, Faruque AS, Mahalanabis D, Hasnat A. Infectious agents causing acute watery diarrhoea in infants and young children in Bangladesh and their public health implications. J Trop Pediatr. 1994 Dec;40(6):351-4.

[16]. Lakshminarayanan S, Jayalakshmy R.Diarrheal diseases among children in India: Current scenario and future perspectives. J Nat Sci Biol Med. 2015 Jan-Jun;6(1):24-8. doi: 10.4103/0976-9668.149073

[17]. Strand TA, Sharma PR, Gjessing HK, Ulak M, Chandyo RK, Adhikari RK. Et al,. Risk factors for extended duration of acute diarrhea in young children. PLoS One. 2012;7(5):e36436. doi: 10.1371/journal.pone.0036436. Epub 2012 May 8.

[18]. Pawlowski SW, Warren CA, Guerrant R. Diagnosis and treatment of acute or persistent diarrhea. Gastroenterology. 2009 May;136(6):1874-86. doi: 10.1053/j.gastro.2009.02.072. Epub 2009 May 7.

[19]. Nguyen TV, Le Van P, Le Huy C, Weintraub A. Diarrhea caused by rotavirus in children less than 5 years of age in Hanoi, Vietnam. J Clin Microbiol. 2004 Dec;42(12):5745-50.

[20]. World Health Organization (WHO) The treatment of diarrhoea: a manual for physicians and other senior health workers. Geneva: WHO 2005. Available from: http://www.who.int/maternal_child_adolescent/documents/9241593180/en/

[21]. Ruxin JN. Magic bullet: the history of oral rehydration therapy. Med Hist. 1994 Oct; 38(4): 363–397. PMCID: PMC1036912.

[22]. Berni Canani R, Buccigrossi V, Passariello A. Mechanisms of action of zinc in acute diarrhea. Curr Opin Gastroenterol. 2011 Jan;27(1):8-12. doi: 10.1097/MOG.0b013e32833fd48a. Review.PMID:**20856116**

[23]. Hoque KM, Binder HJ. Zinc in the treatment of acute diarrhea: current status and assessment. Gastroenterology. 2006 Jun; 130(7):2201-5.

[24]. McFarland LV. From yaks to yogurt: the history, development, and current use of probioticsCurr Opin Gastroenterol. 2011 Jan; 27(1):8-12. Doi:10.1097/MOG.0b013e32833fd48a. Clin Infect Dis. 2015 May 15; 60 Suppl 2:S85-90. Doi: 10.1093/cid/civ054.

[25]. McFarland LV. Systematic review and metanalysis of Saccharomyces boulardii in adult patients World J Gastroenterol. 2010 May 14; 16(18):2202-22.
[26]. Periti P, Tonelli F. Preclinical and clinical pharmacology of biotherapeutic agents: S. boulardii. J Chemother 2001; 13: 473 Verna EC, Lucak S. Use of probiotics in gastrointestinal disorders: what to recommend? Therapy Adv Gastroenterology. 2010 Sep;3(5):307-19. doi: 10.1177/1756283X10373814.
[27]. Kurugöl Z, Koturoğlu G. Effects of Saccharomyces boulardii in children with acute diarrhoea. Acta Paediatr. 2005 Jan; 94(1):44-7.
[28]. Htwe K, Yee KS, Tin M, Vandenplas Y. Effect of Saccharomyces boulardii in the treatment of acute watery diarrhoea in Myanmar children: a randomized controlled study. Am J Trop Med Hyg. 2008 Feb;78(2):214-6.
[29]. Riaz M, Alam S, Malik A, Ali SM. Efficacy and safety of Saccharomyces boulardii in acute childhood diarrhea: a double blind randomisedcontrolled trialIndian J Pediatr. 2012 Apr;79(4):478-82. doi: 10.1007/s12098-011-0573-z. Epub 2011 Oct 14.
[30]. Dinleyici EC, Eren M, Ozen M, Yargic ZA, VandenplasY Effectiveness and safety of Saccharomyces boulardii for acute infectious diarrhea. Expert Opin Biol Ther. 2012 Apr;12(4):395-410. doi: 10.1517/14712598.2012.664129. Epub 2012 Feb 16.
[31]. Burande MA. Comparison of efficacy of Saccharomyces boulardii strain in the treatment of acute diarrhea in children: A prospective, single-blind, randomized controlled clinical trial. J Pharmacol Pharmacother. 2013 Jul; 4(3):2. PMCID: PMC3746305.
[32]. Feizizadeh S, Salehi-Abargouei A, Akbari V. Efficacy and safety of Saccharomyces boulardii for acute diarrhea. Paediatrics. 2014 Jul; 134(1):e176-91.

Dr. Arvind Kumar M.D. Paeds (Specialist,Bgh). “To Study The Role Of Saccharomyces Boulardii In Treatment Of Acute Watery Diarrhea In Children Aged 6 Months To 5years: Prospective Randomized Control Study. ” IOSR Journal of Dental and Medical Sciences (IOSR-JDMS) , vol. 17, no. 3, 2018, pp. 35-40