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

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

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AIM : To study the role of Saccharomyces boulardii in treatment of acute watery diarrhoea in children aged 6 months 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 diarrhoea 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 variables: Duration of diarrhea, Frequency of loose stools.

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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.

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.

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

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.

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 1.87 million. An average Indian child less than 5 years of age will have 2–3 episodes of diarrhoea.

Prevention of all-cases of diarrhoea; rotavirus vaccines are efficacious to prevent diarrhoea specific to rotavirus. Proper hand washing, exclusive breast feeding and use water treatment are effective strategies for prevention of all causes diarrhoea. 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.

Intravenous fluids are required in treatment failures associated with high frequency of stools, uncontrolled vomiting or poor oral intake due to associated infection. 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\textsuperscript{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\textsuperscript{10}.

\section*{II. Review Of Literature}

WHO defines diarrhoea as, passage of \( \geq 3 \) 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\textsuperscript{11}. Diarrhoeal diseases can be classified according to their clinical pattern as:

\begin{itemize}
\item[(i)] acute watery diarrhea (i.e. diarrhea without blood lasting less than 14 days);
\item[(ii)] persistent diarrhea (i.e. diarrhea lasting 14 days or more); or
\item[(iii)] Acute bloody diarrhea (i.e. diarrhea with blood lasting less than 14 days).
\end{itemize}

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)\textsuperscript{12}. The causes of acute diarrhoea in children vary with the location, time of year, and population studied\textsuperscript{13}.

\subsection*{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\textsuperscript{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\textsuperscript{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\textsuperscript{15}. Among the above mentioned risk factors, breastfeeding may be the most important modifiable risk factor for reducing duration of diarrhoea\textsuperscript{16}.

\subsection*{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)\textsuperscript{17}.

\subsection*{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\textsuperscript{18}.

\subsection*{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\textsuperscript{19}.

\section*{III. Oral Rehydration Therapy}

Dr Nobert Hirschhorn, 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\textsuperscript{20}.

\subsection*{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\textsuperscript{21}. It acts as a K channel blocker of adenosine 3', 5'-cyclic monophosphate-mediated chlorine secretion\textsuperscript{22}. 

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DOI: 10.9790/0853-1703083540
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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. S. boulardii survives best at 37°C; 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.

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.

Studies on Saccharomyces:
In a study done by Kurugöl Z, Koturoğlu G 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. 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.

A systematic review and meta-analysis conducted by Dinleyici EC, Eren M, Ozen M, Yargic ZA, VandenplasY et al found the benefits of S. boulardii in decrease in hospital stay and duration of diarrhea in developing countries.

Burande Meeta A, Burande Amit R, 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, 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 diarrhoea 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)

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<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
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</thead>
<tbody>
<tr>
<td>n</td>
<td>Mean ± SD</td>
<td>n</td>
</tr>
<tr>
<td>Frequency of stool on admission</td>
<td>25 12.08 ± 3.58</td>
<td>25 11.6 ± 3.12</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
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<th>Group III</th>
<th>Group IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>Mean ± SD</td>
<td>n</td>
</tr>
<tr>
<td>Frequency of stool on admission</td>
<td>2 10.52 ± 1.71</td>
<td>25 11.16 ± 2.13</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
</tr>
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<tbody>
<tr>
<td>Duration of diarrhea (hrs)</td>
<td>76.32 ± 24.2</td>
<td>95.52 ± 25.09</td>
</tr>
</tbody>
</table>

P Value 0.011
Comparison of mean duration of diarrhea in Group-III and Group IV(block 2)

<table>
<thead>
<tr>
<th></th>
<th>Group III</th>
<th>Group IV</th>
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<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Median (Min - Max)</td>
</tr>
<tr>
<td>Duration of diarrhea (hrs)</td>
<td>77.28 ± 26.17</td>
<td>72(48 - 120)</td>
</tr>
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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

DO: 10.9790/0853-1703083540 www.iosrjournals.org 39 | Page
To Study The Role Of Saccharomyces Boulardii In Treatment Of Acute Watery Diarrhea...


