



CLINICAL EVALUATION OF *NAGARADI* GRANULES IN *BALATISARA* (A STUDY PROTOCOL)

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Abstract-

Atisara is a disease of intestinal disturbances; involves water & electrolyte imbalances, malnutrition. It not only affects health of children but is also considered responsible for infant mortality. *Atisara* explained in *Ayurveda* can be correlated to diarrhea, where *Ati* means excess & *Saranam* means flow; condition where watery stools passed in excess with high speed.

The *Balatisara* affects large number of population worldwide and prevalence of diarrhea now a day's deteriorating school performance of many children. It is a cause of concern for the parents as the as the child will have sunken eyes, flabby skin and look severely ill and weak, even if diarrhea occur day or two. The parents would want the Doctor immediately to stop it with in short duration as there may leads to severe complication in children, if not treated in some tribal places of India parents are unaware of this *Atisara* disease and its treatment and their negligence result in severe dehydration which finally result in death of child, resulting in so many death due to *Balatisara*.

Thus, in present study *Balatisara* is taken as the subject of intervention with the drug '*Nagaradi Granules*' mentioned in *Yog Ratnakara* under *Balrogadhikara*.

MATERIALS AND METHODS: This prospective, open-label, randomized clinical trial will be conducted at, Rishikul Campus, Haridwar of Uttarakhand Ayurved University. A total of 50 children of aged 5-15 years irrespective of gender with classical symptoms of *Balatisara* will be enrolled in the study. The outcome will be assessed according to the subjective and objective parameters established respectively for the study on each visit. Safety will be assessed based on the incidence of adverse events.

DISCUSSION AND CONCLUSION: *Atisara* is the disease of GIT and it has *aaharaj* and *viharaja Nidana* and its *samprapti* involves vitiation of *vata dosha* and *apa dhatu* along with *agnimandya* and *mala dravata*. It occurs mainly due to unhygienic conditions that's why it is found more in children of low socio-economic status. As its *samprapti* involves *agnimandya* and *mala dravata* and the *Ayurvedic* formulation chosen for this study, "*Nagaradi granules*" usually have *deepana*, *pachana* and *grahi* property. So, it is expected that the

outcomes of this trial will suggest probable therapeutic options for the effective management of *Balatisara* of children.

Key words – *Atisara, Ayurveda, Saranam, Nagaradi, Yog Ratnakara, Balrogadhikara, aaharaj, viharaja Nidana, agnimandya, deepana, pachana, grahi.*

CTRI NO.- CTRI/2023/07/055275 (Clinical Trial Registry of India).

INTRODUCTION-

Maintenance and achievement of health and cure the disease of diseased person is the primary aim of *Ayurved* and this has to maintain throughout life.¹ India is counted of the faster developing country the industrial development leader to unhygienic environment, water pollution, air pollution, sound pollution etc. this unhygienic environment along with low economical condition in community are some reason causing any health problem like *Bala-Atisara*. Alteration in consistency or frequency of stool result in a net loss of fluid and electrolytes from the body is termed as *Atisara*.²

The WHO has constituted a diarrheal disease control program, which includes traditional medicinal practices together with the evaluation of health education and prevention approaches.³ A diversity of recognized microorganisms such as bacteria, viruses and parasites can be associated with severe acute infectious diarrhea in children. However, the frequencies of these pathogens vary with geographic region and also depend upon the socioeconomic/sanitary conditions achieved. Several organisms have been implicated as important causes of diarrhea related deaths. The enteric pathogens rotavirus and diarrhoeagenic *Escherichia coli* (DEC) are the most common causes of diarrhea globally,⁴ while DEC has been cited as the most important cause in developing countries.⁵

Atisara is a common ailment of the current era which may be due to irregular and unhealthy habits related to *Ahara* and *Vihara*. *Atisara* explained in *Ayurveda* can be correlated to diarrhea, where 'ati' means excess and 'saranam' means flow i.e., a condition where watery stools passed in excess⁶. '*Balatisara*' is a disease of children mainly involves symptoms of disturbed bowel movements. It affects large number of children population world widely and prevalence of diarrhea now a days deteriorating school performance of many children. Lack of immunity, susceptibility towards the causative pathogens, low hygienic condition, malnutrition and consumption of contaminated food items can cause *Balatisara*.

According to WHO, "Diarrhea is defined as the passage of three or more loose or liquid stools per day (or more frequent passage than is normal for the individual)".⁷

The term ***Balatisara*** is found at first in *Harita Samhita* in context of treatment. The term *Balatisara* literary means *Atisara* occurring in children but it has not been mentioned as a separate entity in *Brihatrayi*. Though several scattered references of term *Balatisara* are found in context of treatment of *Atisara* in children in *Laghutrayi*, *Atisara* (Diarrhea) has been dealt in much detail in *Ayurvedic* literature, but not in term of children specially. The detailed description of *Atisara* in children is not explained in *Ayurveda*. However, in *Kaumarbhritya* certain specific disorder in which diarrhea is major symptom have been mentioned in *Ayurvedic* literature. *Atisara* is described as a symptom in many diseases like *Dantobhedjanyatisara, Ksheeralaska, Vyadhifaka, Revati, Putna, Balagraha* etc. Even though separate description of *Balatisara* as a disease is not found in scriptures, but specific treatment remedies are available there specially for *Balatisara* (Diarrhea in children). The *samprapti* of *Atisara* may be same for both in adult and children but they differ in terms of some added etiological factors (like *Dantobheda, Balagraha, Ksheeralsaka* etc.) and increased morbidity and mortality. The word '*Krimi*' is an important factor for the *Atisara*, in children considered by *Acharya Charaka* and *Acharya Sushruta*. These added etiological factors which differentiates *Balatisara* from *Atisara* are restricted to the infancy period only. Denition diarrhea, lactose intolerance diarrhea, rotavirus diarrhea etc. are some examples of diarrhea which occurs in infancy period only⁸. Increase frequency of defecation, disturbed

electrolyte balance, thirst, weakness, gas formation and abdominal cramps are the common symptoms of *Balatisara*.

Acharya Kashyapa has not separately described *Balatisara* but he has mentioned *Poorvroopa* of *Atisara* in *Vedana Adhdayay* of *Sutrasthan*,⁹ **Acharya Sushruta**¹⁰ and **Acharya Madhava**¹¹ have mentioned 6 types of *Atisara* – *Vataja*, *Pittaja*, *Kaphaja*, *Sannipataja*, *Aamaja* and *Shokaja*, **Acharya Charaka**¹² and **Acharya Vagbhata**¹³ have mentioned 6 types of *Atisara*, wherein 5 types same as *Acharya Sushruta* except *Bhayaja* replace with *Amaja Atisara* and **Acharya Sharangdhara**¹⁴ has mentioned 7 types of *Atisara* – *Vataja*, *Pittaja*, *Kaphaja*, *Sannipataja*, *Bhayaja*, *Shokaja* and *Aamaja*.

Samanya nidana -

Sr. no.	Samanya Nidana	Acharya Sushruta ¹⁵	Bhaav Prakash ¹⁶	Acharya Vagbhata ¹⁷	Acharya Madhav ¹⁸
1.	<i>Atiguru Swabhava, Maatra</i>	+	+	+	+
2.	<i>Atisnigadha Aahara</i>	+	+	-	+
3.	<i>Atiruksha Aahara</i>	+	-	+	+
4.	<i>Atiushana Aahara</i>	+	-	-	+
5.	<i>Atidrava Aahara</i>	+	-	-	+
6.	<i>Virudhasana</i>	+	-	-	+
7.	<i>Ajeerna</i>	+	-	+	+
8.	<i>Ati Ambu Paan</i>	+	-	+	+
9.	<i>Adharneeya Vega Dharana</i>	+	-	+	+
10.	<i>Ritu Viprit Aahara Vihara</i>	+	+	-	+
11.	<i>Bhaya and Shoka</i>	+	+	-	+

Samprapti ghataka-

<i>Dosha</i>	<i>Vata pradhan tridosha</i>
<i>Dushya</i>	<i>Rasa-jaleeya dhatu</i>
<i>Agni</i>	<i>Mandagni</i>
<i>Shrotasa</i>	<i>Purish, anna and udakvaha</i>
<i>Adhistan</i>	<i>Pakvashya</i>
<i>Shrotodushti</i>	<i>Atipravarti</i>
<i>Rogmarg</i>	<i>Madhyam</i>

Material and methods -**Aim of the study-**

1. To evaluate the efficacy of **NAGARADI GRANULES** in **BALATISARA**.
2. To provide an economic, safe and cost effective *Ayurvedic* formulation in the management of **BALATISARA**.

Selection of patients: Patients will be selected on the basis of classical symptoms of *Balatisara* from OPD, PG Dept of *Kaumarbhritya*, Rishikul Campus, Haridwar.

1. **Inclusion criteria:** Children with age between 5 years to 16 years irrespective of their gender and mild to moderate cases of *Balatisara*.
2. **Exclusion criteria:** Children below age of 5 years and above 16 years, case of severe diarrhea, persistent vomiting, severe dehydration, case of worm infestation induced diarrhea and children with known case of children having any long-term illness like T.B, IBS and other metabolic disorders.
3. **Withdrawal criteria:** Aggravation of symptoms, personal matters and LAMA (leave against medical advice).

4. **ASSESSMENT CRITERIA:**

On the basis of subjective parameters –

S.no.	Parameters	Grade 0	Grade 1	Grade 2	Grade 3
1.	मुद्गुद्गु प्रवृत्ति (Frequency of stool)	1-3 loose stools per day	4-6 loose stools per day	7-9 loose stools per day	>10 loose stools per day
2.	उदरशूल (Abdominal pain)	No abdominal pain	Occasionally	Mild pain	Moderate pain
3.	अतिद्रव मल प्रवृत्ति (Consistency)	Normal	Sometimes hard and sometimes soft stool	Semi – solid stool	Watery stool
4.	अग्निमांघ्र (Decreased appetite)	Normal hunger	Hunger sensation after 4-6 hours of food intake	Hunger sensation after 7-10 hours of food intake	No sensation of hunger after >10 hours of food intake
5.	दुर्गन्धित मल (Foul smell)	Normal	Mild offensive	Moderate offensive	Highly offensive

OBJECTIVE CRITERIA: Consistency and smell

SAMPLE SIZE: Based on the sample size calculation, the sample size is estimated to be 226.8, due to less duration of study time and financial limitations, we will be limiting our sample size to 50.

TYPE OF THE STUDY: Open label single clinical trial.

LEVEL OF STUDY: OPD level

DURATION OF STUDY: 18 months

ASSESSMENT AND FOLLOW UP:

- ✓ With drug – 7 days (On daily basis)
- ✓ Without drug – 7 days
- ✓ Follow up will be done after 7 days of cessation of medicine.

METHOD OF TREATMENT:

1. **Selected drug:** Nagaradi Granules
2. **Form of medicine:** Granules
3. **Composition of medicine:** Nagara, Ativisha, Mustaka, Indrayava

• नागरातिविषामुस्ताबालकेन्द्रयवैः श्रुतम् ।

कुमारं

पाययेत् प्रातः सर्वातीसारनाशनम् ।।

(योगरत्नाकर उत्तरार्द्ध बाल रोगाधिकार 7)

Serial no.	Name of the drug	Proportion	Part used
1.	नागर	1 भाग /1 part	कंद
2.	अतिविषा	1 भाग /1 part	मूल
3.	मुस्ता	1 भाग /1 part	कंद
4.	इंद्रयव	1 भाग /1 part	बीज

Panchbhautika guna of the drug-

1. **Nagara**, *Zingiber officinale* due to *Laghu* and *Snigdha* guna, *Katu rasa*, *Madhur vipaka* and *Ushan veerya* acts as *Kapha- Vata shamaka*, *Triptighana*, *Rochana*, *Deepana*, *Pachana*, *Vatanulomana* and *Shoolprashmana*.
2. **Ativisha**, *Aconitum heterophyllum* due to *Laghu* and *Ruksha* guna, *Tikta* and *Katu rasa*, *Katu vipaka* and *Ushan veerya* acts as *Tridoshara*, *Deepana*, *Pachana* and *Grahi*.
3. **Musta**, *Cyperus rotundus* due to *Laghu* and *Ruksha* guna, *Tikta*, *Katu* and *Kashaya rasa*, *Katu vipaka* and *Ushan veerya* acts as *Kapha-pitta shamaka*, *Deepana*, *Pachana* and *Grahi*.
4. **Indryava**, *Holarrhena antidysnterica* due to *Laghu* and *Ruksha* guna, *Tikta* and *Kashaya rasa*, *Katu vipaka* and *Sheeta veerya* acts as *Kapha-Pitta Shamaka*, *Deepana*, *Stambhaka*, *Pravahika-Nashaka* and *Sangrahi*.

Drugs and their pharmacological actions -

DRUG	PHARMACOLOGICAL ACTION
• <i>Nagara</i>	Appetite stimulant, Antioxidant, Anti-inflammatory and Anti-emetic actions.
• <i>Ativisha</i>	Antipyretic, Stomachic, Antiemetic, Anthelmintic, Antidiarrheal, Carminative, Anti-inflammatory and Antimicrobial
• <i>Musta</i>	Anti-diarrheal, Anti-inflammatory, Anti-emetic, Analgesic, Antipyretic, Gastroprotective activity, Antiseptic properties and Inhibition of gastric motility activity.
• <i>Indrayava</i>	Anti-diarrheal, Anti-bacterial, Anti-protozoal, Antispasmodic, Anti-amoebic activity.

- 4. Route of administration:** Oral
- 5. Preparation of medicine:** Identification of the drugs will be done in *Dravyaguna* department & preparation will be done in *Ras Shastra Evam Bhaisjya Kalpana*. Drug will be prepared according to method of preparation of Granules.
- 6. Storage of medicine:** The medicine will be stored in air tight containers.
- 7. Drug dose:** For present study, I have taken drug doses of *Nagaradi* granules according to *Sharangdhara Samhita*. One *Masha* for one year child and these *1 Masha* increases every year, upto 16 years. Thus, for the age of 04- 16 years the dose will be 04 *Masha* to 16 *Masha* in divided dose. (1 *Masha* =1gm)

Age (in years)	Dose (two divided doses)
5 years	5 gm
6 years	6 gm
7 years	7 gm
8 years	8 gm
9 years	9 gm
10 years	10 gm
11 years	11 gm
12 years	12 gm
13 years	13 gm
14 years	14 gm
15 years	15 gm
16 years	16 gm

Safety Outcomes

Safety will be assessed based on the occurrence of adverse events on each follow-up visit. The adverse events, if any, will be recorded as per Good Clinical Practice guidelines.

Ethical considerations

The study is approved by the Institutional Ethics Committee of the Uttarakhand Ayurved University, Rishikul Campus, Haridwar. Written informed consent will be obtained from the parents of eligible children by the investigator before enrollment.

DISCUSSION AND CONCLUSION –

Globally, diarrhea is the second largest cause of death in children under 5 years of age, causing one in every five deaths. Unfortunately, diarrhea kills more children than AIDS, malaria and measles combined.¹⁹ In India, 13% of the 1.8 million under 5 years of age death is because of diarrhea, accounting for more than 2, 37, 000 children a year which is almost one fifth of global child mortality.²⁰ So, there is a need of reliable, safe and cost-effective formulation for *Balatisara* in *ayurveda*. Therefore, *Nagaradi* granules described by *Acharya Yog Ratnakar* for *Balatisara* has been selected has been selected for the study. The formulation includes contents like *Nagara* (*Zingiber officinale*), *Ativisha* (*Aconitum heterophyllum*), *Musta* (*Cyperus rotundus*), *Indryava* (*Holarrhena antidysenterica*) which have stomachic, antidiarrheal, carminative, anti-inflammatory, antimicrobial, gastroprotective activity, inhibition of gastric motility activity and antispasmodic properties respectively which will help in breaking the *samprapti* of *Balatisara*. Antidiarrheal activity of *Kutaja* may be because of its specific action as antiparasitic activity against *E. histolytica* and *G. Lambalia*;²¹ antibacterial effect on *E.coli* etc,^{22,23} which can be correlated with Hetu *Viprita Upashaya* (allaying disease by diet, drug and regimen) as indicated by Chakrapani.²⁴

Indrayava (*H. antidysenterica*-Wall) is well known for its antidiarrheal and antidysenteric activity, attributable to its pharmacodynamic properties viz. *Kapha-Pitta-Rakta Samgrahika* (enhance uniform absorption), *Upashoshana* (astringent property),²⁵ *Katu-Kashaya Rasa* (pungent-astringent taste), *Ruksha* (dry), *Deepana* (appetizer) and *Amahara* (allays indigestion).^{26,27} The elimination of mucus and subsidence of abdominal pain is due to its anti-inflammatory and analgesic properties.^{28,29}

Thus, it is expected that *Nagaradi* granules will promising results in children with manifestation of *atisara*.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest

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