Evaluation of comparative efficacy of Withania Somnifera treated milk decoction enema with Tribulus Terrestris treated milk decoction enema in Undernutrition - Randomized controlled trial a Protocol

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Abstract

Background: Undernutrition is one of the eight socially despicable, or as said in Charak Samhita, it is one of the eight undesirable conditions (Ashtau ninditiya purush) mentioned by Acharya Charaka . When the body gets emaciated gradually over time, that condition is known as Karshya. It is a nutritional deficiency. It is a condition with poor absorption, excessive loss of nutrients, or inadequate food consumption. Food is one of the three main pillars of life. Karshya can be correlated with undernutrition. As Rasa Dhatu (which can be correlated with plasma) is not produced correctly, due to which following Dhatu also gets affected and leads to undernutrition

Objective: To compare the efficacy of Tribulus Terrestris-treated milk decoction enema and whitania somnifera-treated milk decoction enema in undernutrition with criteria like total body weight, body mass index, and anthropometric measurements.

Methods: - In this study, 60 patients will be divided into two groups. In Group, A will be whitania somnifera treated milk decoction enema will be administered in the dose form of 200ml for eight days .The same will be used for the other 30 patients, i.e., group B with Tribulus Terrestris treated milk decoction enema.

Results: The result will be assessed on the baseline of objective parameters, and data will be compared after the treatment

Conclusions: To be based on observations and results obtained. Clinical Trial: CTRI No. - CTRI/2022/12/048024 (clinical trial registry India)

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Evaluation of comparative efficacy of Withania Somnifera treated milk decoction enema with Tribulus Terrestris *treated milk decoction enema* in Undernutrition - Randomized controlled trial a Protocol

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(Clinical Trial Registry India)

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Introduction –

In today's modern world, many people suffer from lifestyle disorders like obesity, hypertension, diabetes, etc. But one such disorder that mostly goes unseen is undernutrition. It is one of the eight socially despicable or, as written Ayurvedic text *Charak Samhita*, one of the eight undesirable conditions mentioned in Ayurvedic text *Charaka Samhita* [1]. When the body gets emaciated

gradually over time, that condition is known as undernutrition. It is a nutritional deficiency. It is a condition in which there is poor absorption, excessive loss of nutrients, or inadequate food consumption. Food is one of the three pillars of life [2]. Many factors are responsible for undernutrition, such as low intake of food or inadequate intake of nutritional food, malabsorption of food, the excessive output of waste due to some underlying conditions, and some chronic diseases that can also lead to undernutrition. Factors that lead to Undernutrition as written in ayurvedic texts are intake of food or drinks that are dry, fasting, less intake of food, grief, anger, worries, fear, excessive mental and physical activity, excessive evacuation therapy (*excess* of panchakarma), excess dry anointing to the person, stopping or suppressing the natural urges like sleep, hunger, and thirst, excessive sexual intercourse, excess bath, the natural constitution of the person's, heredity, old age[3] are some factors making the person lean. Undernutrition is a disease that reduces body mass. It is caused by [4] reduced *rasa Dhatu* (the component of the body with nutrients and essence, which can be correlated with plasma). As plasma (*Rasa Dhatu)* is not appropriately produced in this condition, other tissue (*Dhatu)* also gets affected and causes undernutrition. People affected with undernutrition have the following symptoms as written in ayurvedic texts– [5] dried or malnourished buttocks, neck, and abdomen, vascular network is prominently seen, a thin layer of skin on the bone is seen, a person cannot tolerate physical exercise *[6]*, a person cannot tolerate hunger, thirst, diseases, cannot tolerate too much of cold or heat and sexual intercourse. Vitiation of power of movement (*Vata)* takes place, which leads to impaired digestive fire. Impaired digestive power leads to the formation of undigested food. All of this leads to inadequate and improper plasma (*Rasa Dhatu)* absorption due to the formation of undigested food (*Ama Ahara)*. This leads to insufficient nourishment of tissue. As undernourished plasma (*Rasa Dhatu)* is circulated all over the body, other tissues (*Dhatus)* do not get nutrition due to decreased and dried plasma (rasa dhatu).

Tribulus Terrestris is a drug mentioned in the ayurvedic text- *Bhavapraksha* of *Bhavmishra In Purvakhanda Haritykadi Varga[7]. Taste (Rasa), potent energy (Virya), and a post-digestive effect (vipaka)* of Tribulus Terrestris are *sweet (Madhura), cold (Shita) &sweet (Madhura),* respectively. These sweet tastes (*Madhura Rasa), cold potency (Sheeta Virya),* and sweet post-digestive effects (*Madhura Vipaka)* are said to be body mass enhancers (*Bruhaniya)* in nature.

Withania Somnifera *(Ashwagandha)* [8] is a commonly used drug as a body mass enhancer(*Bruhana*). Taste (Rasa*),* potent energy *(Virya*), after digestive effect *(vipaka)* of Withania Somnifera, is bitter (*Tikta rasa),* astringent *(Kashaya Rasa), hot (Ushna Virya),* sweet *(Madhur Vipaka)*.

Cow milk is said to be having anti-aging effects. It gives power *and* improves *mind power.[9]*

The rectal route for drug delivery may be advantageous for medications whose oral administration

results in poor stability, solubility, or permeability. Additionally, it can be used when oral ingestion is impossible, such as when a patient is experiencing nausea and vomiting, is unconscious, or has trouble swallowing. The environment in the empty rectum is thought to be relatively steady and stable despite the rectum's surface area being significantly smaller than that of the small intestine. Compared to other parts of the gastrointestinal tract, this one favors a repeatable absorption process and has minimal enzymatic activity. Additionally, after systemic absorption, drugs may partially bypass the liver, which lessens the hepatic first-pass effect. [10]

Objectives –

Primary Outcome- we will assess the effect of interventional drug enema on BMI, Weight & anthropometric measurements.

Secondary Outcome – To assess and compare the efficacy of standard and controlled drug in the study.

Trial Design -

Randomized standard controlled single-blind superiority clinical trial**.**

This will be a parallel group trial. The trial will include 60 patients and treatment of 8 days with follow-up on the 8^{th},12^{th} & 24^{th} day.

For protocol purposes and according to the calculated sample size for each group is = **52**

But for study purposes, we will be taking a sample size of 30 in each group as there is a limited time duration of the study and by considering the economic aspect of the study.

Methods: Participants, interventions, and outcomes

Study Setting

The patients of undernutrition (*Karshya)* will be selected from the Panchakarma OPD and IPD of Mahatma Gandhi Ayurved College, Hospital & Research Centre, Salod (H), and from specialized peripheral camps.

Eligibility Criteria - Patients willing to give written consent

Either gender, age 18-50 years

BMI ≤ 18.5 Kg/m^2 [11]

Subjects having symptoms of undernutrition

Interventions: Group A – Whitania somnifera treated milk decoction enema for 8 days before a meal (empty stomach) once a day in the morning will be administered.

Group B- Tribulus terrestris treated milk decoction enema for 8 days before a meal (empty stomach) once a day in the morning will be administered.

Preparation – **Whitania somnifera treated milk decoction enema (Group -A)**

1. Process of milk decoction -

One part of the drug (19 gm) is added in 8 parts of milk (152 ml) and then 32 parts of water(608 ml). Then boiling is continued till the added water gets evaporated and the original quantity of milk(i.e., 152 ml) is left (1:8:32). It has to be prepared on low flame(*Mandagni)* so that sensitive active principle may not get spoiled with high temperature. [12]

2. Preparation of Whitania somnifera-treated milk decoction enema-

Preparation *of* Whitania somnifera treated milk decoction enema: First, honey(17 gm) was added, then rock salt(1gm) was added and thoroughly triturated with a wooden churner. Finally, clarified butter*(25 gm)* was warmed and slowly added. After the clarified butter had been well blended, a proportionate amount of withania somnifera powder(8gm) & water was added, and the mixture was thoroughly triturated again. The next step was to add the milk decoction, as mentioned above. A colloidal solution was made by simply mixing all of the ingredients.

***Tribulus Terrestris* treated milk decoction enema (Group -B) –**

1. Process of milk decoction -

One part of the drug (19 gm) is added in 8 parts of milk (152 ml) and then 32 parts of water (608 ml). Then boiling is continued until the added water evaporates and the milk's original quantity (i.e., 152 ml) is left (1:8:32). It has to be prepared on low flame so that sensitive active principle may not get spoiled at high temperature. [12]

2. Preparation of Tribulus Terrestris *treated milk decoction enema* -

Preparation *of Tribulus Terrestris treated milk decoction enema*: First, honey(17 gm) was added, then rock salt(1gm) was added and thoroughly triturated with a wooden churner. Finally, clarified butter*(25 gm)* was warmed and slowly added. After the *clarified butter* had been well blended, a proportionate amount of Tribulus Terrestris powder(8gm) and water was added, and the mixture was thoroughly triturated again. The next step was to add the Ksheerapaka, as mentioned earlier. A colloidal solution was made by simply mixing all of the ingredients.

Criteria for Discontinuing or Modifying Allocation Intervention:

Subjects will be withdrawn from the trial if any unintended occurrence, signs of medication sensitivity, or any other disease or problem emerges, and free therapy will be supplied to the person

until the difficulty subsides. we will assess the patients after administration of Enema for any unwanted symptoms in order to assess and monitor drug adherence, and the subject will be monitored throughout the therapy.

Primary Outcome- we will assess the effect of interventional drug enema on BMI, Weight & anthropometric measurements.

Secondary Outcome – To assess and compare the efficacy of standard and controlled drug in the study.

Objectives – Body mass index, Weight, Anthropometric measurements (before and after treatment). Evaluation of the above parameters will be done on the 0th (before treatment),on the 12th day, and on the 24th day(after treatment). intervention strategy will be overseen by the investigator, who will keep a record of their progress in proper paperwork.

Plan to ensure that participants are retained and that all follow-ups will be completed: We will keep in touch with the patients by capturing their phone numbers and providing timely medicine and follow-up guidance, with the data from the follow-up being stored in the paperwork with justification.

Participant timeline -

Scholar/ Investigator	Dr.Ashwin k. Gokhare					
Title	Evaluation of comparative efficacy of Withania somnifera treated milk decoction enema with Tribulus Terrestris *treated milk decoction enema* in Undernutrition - Randomized controlled trial					
Steps	Q1	Q2	Q3	Q4	Q5	Q6
Approval from IEC						
Review of Literature						
Drug Preparation						
Enrollment of the patients						
Data Collection						
Statistical Analysis						
Thesis writing						
Submission						

Sample size- Formula Using Mean Difference

n1 = n2 =2 (Z α **+ Z** β ¿2σ ²

$$(\delta)^2$$

Primary variable (body weight)

Mean (Pre) results on body weight for the experimental group = 42.5

Mean (Post) results on body weight for the experimental group =47.6

Difference = 5.1 (As per reference article) in the control group

Considering 20% clinically relevant superiority difference =(5.1 *20) = 1.02

standard deviation σ = 1.65

As per reference articles,

$$N1 = \mathbf{n1 = n2 = \frac{2\,(1.96 + 0.84)^2 (1.65)^2}{(1.02)^2}}$$

=52

Notations:1

Zα = 1.96

α = 5% Level of Significance

Zβ = 0.84 at 80% power

Reference article – Clinical evaluation of Ksira Basti and KsiraPaka of Balya drugs on Karshya

Recruitment:

By simple random sampling method, 60 patients will be recruited (30 in each group)

Implementation:

The Principal Investigator will enroll and allocate the patient.The patients of *Karshya* will be selected from the Panchakarma OPD and IPD of Mahatma Gandhi Ayurved College, Hospital & Research Centre, Salod (H), and from specialized peripheral camps.

Allocation sequence generation – computer-generated random numbers.

Allocation implementation – the researcher or the first author will generate an allocation sequence, enroll participants, and assign participants to intervention.

Blinding - single-blind superiority clinical trial**.**

Data collection plan –

Study instruments –

1. *Ayurveda Samhitas*

2. Modern texts
3. Online search- Google Scholar, etc.
4. *Gokshura siddha kshir Basti*
5. *Ashwagandha siddha kshir Basti*
6. Case record form
7. Patient information
8. Written and informed consent form
9. Measuring scale
10. Sphygmomanometer
11. Weighing machine
12. Enema catheter
13. Enema pot
14. Measuring tape
15. Vernier caliper

Drug collection/ authentication-The raw material for the drug will be purchased from a reliable source and will be authenticated and identified by the department of Dravyaguna and *Rasashastra* of M.G.A.C.H. and RC, Salod, Wardha, Maharashtra ,India. Milk will be collected fresh from an authenticated cow milk provider.

Statistics outcome – after the study data will be analyzed according to a suitable statistical test.

Data Analysis (statistical methods)- The collected data will be analyzed with the help of an inferential statistical test.

Data monitoring: formal committee - The study will start after clearance from the I.E.C. of Mahatma Gandhi Ayurved College Hospital and Research Centre, Salod (H), Wardha. And after CTRI registration.

Ref. No. MGACHRC/IEC/JULY – 2022/553

Clinical Trial Registry India - CTRI/2022/12/048024

The committee will decide on the endpoint and oversee the trial as it progresses. The researcher will assess any adverse event and will report to the Ethics Committee.

Dissemination – This protocol will be further published as a thesis to disseminate the study of undernutrition. The study protocol provides a detailed overview of the study design, methodology, data collection procedures, data analysis plan, and ethical considerations. By disseminating this protocol, we hope to advance knowledge in the field and facilitate future research.

Guidelines – SPIRIT Guidelines are being used for the study.

Consent -Patients' consent will be taken before conducting the trials in the local language while explaining every aspect of the study. The researcher will obtain consent from trial participants. Consent forms and other related documentation are given to Participants.

The personal information of the participants will be collected and kept confidential before, during, and after the trial. Physical Data will be stored in a protected storage facility with only access to the researcher. Computerized data will be held in a password-protected hard drive with only access to the researcher.

Reference –

1. Acharya Vidyadhar Shukla. Charak Samhita. Chaukhamba Sanskrit Pratishthan; 2016. Sutra Sthana, Chapter 21, Verse 3.
2. Agnivesha, Charak Samhita, with Charak Chandrika Hindi commentary, by Dr Tripathi Brahmanand and Dr Pandey Ganga Sahay. Chaukhamba SurbhartiPrakashan; 2007. Sutra Sthana, Chapter 11, Verse No. 34, p. 238.
3. Acharya Vidyadhar Shukla. Charak Samhita. Chaukhamba Sanskrit Pratishthan; 2016. Sutra Sthana, Chapter 21, Verse 11-12.
4. Sushrut Samhita, edited with Ayurveda-tattva-sandipika, Hindi commentary, Kaviraj Ambikadutta Shastri Part 1. Chaukhamba Sanskrit Sansthan; 2020. Sutra Sthana, Chapter 15, Verse 16.
5. Acharya Vidyadhar Shukla. Charak Samhita. Chaukhamba Sanskrit Pratishthan; 2016. Sutra Sthana, Chapter 21, Verse 13-14.
6. Shri Bhavprakash, Madhyamottarkhanda, Ayurved Acharya Shri Hariprasad Pandayen. Chaukhama Sanskrut Series; 1998. Chapter 40, Verse 3.
7. Bhahavprakash Nighantu of Bhavamishra, commentary by Prof. K.C.Chunekar. Chaukhamba Bharti Academy; 2016. Verse 4/39.
8. Bhahavprakash Nighantu of Bhavamishra, commentary by Prof. K.C.Chunekar. Chaukhamba Bharti Academy; 2016. Guduchyadi varga, Verse 161-162.
9. Vagbhata. Ashtanga Hridayam, edited with Nirmala Hindi commentary by Dr. Brahmanand Tripathi. Chaukhamba Sanskrit Pratishthan; 2019. Sutrasthan 5, Verse 20-22.
10. Hua S. Physiological and Pharmaceutical Considerations for Rectal Drug Formulations. Front Pharmacol. 2019 Oct 16;10:1196. PMID: 31680970; PMCID: PMC6805701. doi: 10.3389/fphar.2019.01196.
11. Lim JU, Kim JH, Jung CY, et al. Comparison of World Health Organization and Asia-Pacific body mass index classifications in COPD patients. Int J Chron Obstruct
12. Murthy, K. R. S. (2009). Translation of Sharangadhara Samhita Madhyama Kanda (Chapter 2/161). Chaukhambha Orientalia Varanasi.

Supplementary Files

CONSORT (or other) checklists

SPIRIT Checklist.
URL: http://asset.jmir.pub/assets/bc912600f0aca495a37f4c6e446548bb.pdf