



Preclinical Evaluation of Standard Ksharsutra Ingredients on Causative Organisms of Bhagandara and Comparative Study of Efficacy of Modified & Standard Ksharsutra on Bhagandara W.S.R. To Fistula-In-Ano ---A Study Protocol

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Abstract

The word *Ksharsutra* comprises of two words i.e., *Kshar* which means a special medicine that is alkaline in nature and is derived from the ashes of certain plants like *Apamarga* (*achyranthes aspera*) *Yava* (barley), etc. and *Sutra* means a thread. So *Ksharsutra* is a specialized medicated thread.

Even after too much advance in the surgical specialty; modern health science fails to manage Fistula-in-Ano effectively. In this scenario, Ksharsutra treatment becomes a ray of hope for patients suffering from Fistula-in-Ano.

Aim & Objective: To study the Phytochemical and anti-microbial properties of *Ksharsutra* formulation on causative micro-organisms of *Bhagandara*, and to compare the efficacy of standard and modified *Ksharsutra* in *Bhagandara* W.S.R to Fistula-in-Ano.

Methodology: Ingredients of Standard *Ksharsutra* are being analyzed Phytochemically & Anti-microbially.

For the duration of healing of the Fistula tract, 60 patients are being enrolled out of which 30 pts are to be treated with standard *Ksharsutra* and another 30 are being treated with modified *Ksharsutra*.

Results: Changes are to be ascertained based on subjective and objective parameters.

Keywords: Bhagandara, Fistula-in-Ano, *Ksharsutra*

INTRODUCTION

Ayurveda literally means ‘Science of life’ [1]. It is one of the world’s oldest holistic healing systems. *Shalya Tantra*, one of the *Asthangas* of *Ayurveda* [2] is gaining popularity among the masses.

The word *Ksharsutra* comprises of two words i.e., *Kshar* which means a special medicine that is alkaline in nature and is derived from the ashes of certain plants like *Apamarga* (*achyranthes aspera*) *Yava* (barley), etc. and *Sutra* means a thread. So *Ksharsutra* is a specialized medicated thread.

Acharya Chakradatta has given the idea about the preparation and use of *Ksharsutra* for the first time [3], but the use of *Kshar* in the preparation of this thread has not been mentioned by him.

भावितं रजनीचूर्णेः स्नुहीक्षीरे पुनः पुनः ।
बन्धनात् सुदृढं सूत्रं भिनत्त्यर्शो भगन्दरम् ॥

चक्रदत्त अर्शोधिकार [3]

Later, extensive work has been done in the department of *Shalya* of Banaras Hindu University regarding the use of *Ksharsutra* in the management of *Bhagandar* (Fistula-in-Ano). After long research the standard *Apamarga Ksharsutra* was developed by *Shalya-Shalakyas* department of Banaras Hindu University which was also approved by Indian Council of Medical Research (ICMR). This procedure involves coatings of *Snuhi Ksheer* (Latex of *Euphorbia neriifolia*); *Apamarga Kshar* (*Kshar* obtained from ashes of *Achyranthes aspera*) and *Haridra* (*Curcuma longa* powder).

Later, the efficacy of *Ksharsutra* treatment in Fistula-in-Ano has been confirmed by clinical trials conducted by ICMR at AIIMS, New Delhi; PGI Chandigarh and other premier

institute of medical education.^[4] But it is not known till date which active principles of the said *Ksharsutra* formulation are working in this treatment.

In this study; it is being tried to find out which are these active principles of *Ksharsutra* formulation.

HYPOTHESIS

Are *Ksharsutra* ingredients and formulation effective on causative micro-organisms responsible for *Bhagandara*; and is there any difference in efficacy of treatment with modified *Ksharsutra* in *Bhagandara* W.S.R to Fistula-in-Ano

➤ Null Hypothesis (H₀)

Ksharsutra ingredients & formulation do not possess Anti-microbial properties on causative micro-organisms of *Bhagandara*; and there is no difference in efficacy of standard and modified *Ksharsutra* in *Bhagandara* W.S.R to Fistula-in-Ano.

➤ Alternate Hypothesis (H₁)

Ksharsutra ingredients & formulation possess Anti-microbial properties on causative micro-organisms of *Bhagandara*; and there is significant difference in efficacy of standard and modified *Ksharsutra* in *Bhagandara* W.S.R to Fistula-in-Ano.

AIMS & OBJECTIVES

Aim

To study Phytochemical and anti-microbial properties of *Ksharsutra* formulation on causative micro-organisms of *Bhagandara*; and to compare the efficacy of standard and modified *Ksharsutra* in *Bhagandara* W.S.R to Fistula-in-Ano.

Objectives

- To identify the phytochemical principles of *Ksharsutra* formulation.
- To evaluate the anti-microbial properties of *Ksharsutra* ingredients and formulation against causative micro-organisms of *Bhagandara* W.S.R to Fistula-in-Ano.
- To find out the mode of action of *Ksharsutra* treatment in *Bhagandara* (Fistula-in-Ano).
- To identify the active principle of *Ksharsutra* formulation so as to make a way for further studies for faster and more convenient treatment.
- To compare the efficacy of standard and modified *Ksharsutra* in *Bhagandara* W.S.R to Fistula-in-Ano.

MATERIAL AND METHODS:

Methodology for Phytochemical & anti-microbial evaluation of standard *Ksharsutra* ingredients.

Experimental:

- Phytochemical analysis
- Anti-microbial analysis

Source of Sample collection:

- Strains:
 - Department of Microbiology, Kurukshetra University; Kurukshetra
 - CSIR-IMTECH, India- Chandigarh
- Herbs:
 - Fresh *Snuhi Ksheer* is being collected from the herbal garden of Shri Krishna Govt. Ayurvedic College, Kurukshetra, Haryana
 - *Kshara* is being prepared from the whole plant of *Apamarga* and
 - Raw *Haridra* rhizome procured from the market and then powdered.

List of Phytochemicals Assay – Qualitative & Quantitative:

- Total flavonoid content
- Total alkaloid content
- Total phenolic content
- Total tannin content
- Total saponin content

Place where phytochemical & anti-microbial study is being conducted:

- Research & Innovation Department, Shri Krishna Ayush University; Kurukshetra
- Department of Microbiology, Kurukshetra University; Kurukshetra

Methodology for Open Interventional Clinical Study to Compare Efficacy of Standard & Modified *Ksharsutra* in *Fistula-in-Ano*:

SOURCE OF DATA-

➤ Clinical Source

Daily Out Patient Department (OPD) & In Patient Department (IPD) based patients of Shri Krishna Govt. Ayurvedic College and Hospital, Kurukshetra and patients diagnosed as *Bhagandara* (*Fistula-in-Ano*) are being considered for the study after obtaining written informed consent.

- **Literary Source**

Ayurvedic samhita and medical text books related to *Bhagandar* (Fistula-in-Ano); and *Ksharsutra* treatment; articles and journals, research paper etc. are being screened for information regarding the subject.

- **Experimental Source**

- Out Patient Department (OPD) & In Patient Department (IPD), Department of Shalya Tantra; Shri Krishna Govt. Ayurvedic College & Hospital; Kurukshetra.

Method of Standard *Ksharsutra* Preparation and to determine the weight of individual ingredient of *Ksharsutra* coated on thread:

- As per the literature; standard *Ksharsutra* is being prepared by 11 coatings of *Snuhi* latex (*Euphorbia neriifolia*), 7 coatings of *Snuhi latex* and *Apamarga Kshara* (*Achyranthes aspera*) and last 3 coatings of *Snuhi latex* and *Haridra Powder* (*Curcuma longum*).
- While preparing the standard *Ksharsutra*; thread is being weighed before application of coatings of standard *Ksharsutra* ingredients.
- Thread is being weighed again after application of every coating.
- In this way; we are able to find out the standard proportion of individual ingredient coated on the thread.

Method of Modified *Ksharsutra* Preparation:

- A mixture is being prepared with the above ingredients of *Ksharsutra* in the proportion as discovered while preparing standard *Ksharsutra*.
- Coating of above said mixture is being done on thread
- Coatings are being repeated after drying of the previous one until modified *Ksharsutra* is prepared having same weight of ingredients as in standard *Ksharsutra*.

Clinical Trial:

- Two group are being made each with 30 patients suffering from Fistula-in-Ano.
- Group A is being treated with Standard *Ksharsutra*.
- Group B is being treated with modified *Ksharsutra*.
- Efficacy of Standard and modified *Ksharsutra* is being evaluated on different parameters.

INFORMED CONSENT –

The study is being explained clearly to the subjects in bilingual language (Hindi & English) and their signed, written, informed consent is being taken before starting the trial.

Sample Selection Criteria

a) Inclusion criteria

- Patients with sign & symptoms of *Bhagandara* (Fistula-in-Ano)
- Irrespective of age, sex, occupation & religion
- Willingness of patients for study

b) Exclusion criteria

- Fistula-in-ano associated with one or more of the following conditions:
 - Tuberculosis,
 - Hypertension,
 - Diabetes mellitus,
 - Osteomyelitis of hip bones,
 - Acute or chronic ulcerative colitis,
 - Crohn's disease,
 - Ano-rectal and other Malignancy,
 - Positive cases of Venereal diseases,
 - HIV and HBsAg,

C) Criteria For Withdrawal –

- Patients reporting with any of the following-
 1. Patients willing to quit in between is being allowed to quit and is being replaced.
 2. If any acute illness or complications develops, patient is being treated accordingly and is being excluded from the study.

STUDY DESIGN –

The study design is as follows:

- **Study type** : Interventional
- **Sub-type** : Open Clinical trial
- **Purpose** : Treatment
- **Timing** : Prospective
- **Masking** : Open trial
- **Sampling Method** : Simple Random
- **End Point** : Efficacy

- **Sample Size** : 60 patients

STATISTICAL CALCULATIONS

Appropriate statistical methods are being used to analyze the data collected in the above observations and suitable conclusion drawn with the consultation of statistician. It is to evaluate the phytochemical and anti-microbial properties of standard *Ksharsutra* ingredients for causative organisms of *Bhagandara* and to compare efficacy of standard & modified *Ksharsutra* in *Bhagandara* W.S.R to Fistula-in-Ano.

INVESTIGATION

- Routine hematological investigations like HB%, TLC,DLC, ESR, Blood grouping , BT, CT
- Random Blood sugar
- HIV, HBsAg, HCV

ASSESSMENT CRITERIA

ASSESSMENT CRITERIA FOR ANTI-MICROBIAL EVALUATION

Effect of active principals of standard *Ksharsutra* ingredients on causative micro-organisms of *Bhagandara* W.S.R. Fistula-in-Ano

ASSESSMENT CRITERIA FOR COMPARETIVE STUDY OF EFFICACY OF STANDRAD & MODIFIED KSHARSUTRA:

Subjective Criteria

Grade = 0	No Pain
Grade = 1	Mild Pain, can be tolerated without any medication
Grade = 2	Moderate Pain, requiring oral analgesics
Grade = 3	Severe Pain, not reliving with oral analgesics and required injection

Table 1: Table 1 Showing Gradation for Pain

Grade = 0	No Discharge
Grade = 1	Mild Discharge (wets 1X1cm gauze piece)
Grade = 2	Moderate Discharge (wets 2X2 cm gauze piece)
Grade = 3	Profuse Discharge (wets more than 2X2 cm gauze piece)

Table 2 Showing Gradation for Discharge

Grade = 0	No Itching
Grade = 1	Negligible Itching with 10-12 hrs gap
Grade = 2	Occasional Itching with 4-6 hours gap
Grade = 3	Frequent Itching with 2-3 hours gap

Table 3 Showing Gradation for Itching

Grade = 0	No Swelling
Grade = 1	Swelling within 1×1 cm
Grade = 2	Swelling within 2 ×2cm
Grade = 3	Swelling within 3×3 cm

Table 4 Showing Gradation for Swelling

Objective Criteria**Unit Cutting Time (UCT)**

UCT=

Total number of days required for complete cutting of tract

 Initial length of thread (tract) in cm

= days/cm

U.C.T.= Time taken (in days) to cut one centimetre of fistulous tract with simultaneous healing

CRITERIA FOR OVERALL RESULT ASSESSMENT:

The overall effect was assessed based on relief in signs and symptoms as below:

- Complete remission:91-100% relief
- Marked improvement:76- 90 % relief
- Moderate improvement:51- 75 % relief
- Mild improvement: 26- 50% relief
- Unchanged: <25% relief

FOLLOW UP

During the *Ksharsutra* therapy, patients are called on every week for *Ksharsutra* changing viz. Day 0, Day 7, Day 14, Day 21, Day 28 and after cut through of the fistulous tract, patients are called for follow up assessment on 7th day, 15th day, and after one month.

ASSESSMENT OF RESULT

Assessment of the result is as per the following criteria:

- **Cure** – 100% free from cardinal signs and symptoms, these are pain, swelling, discharge, itching, local tenderness, length of tract etc.
- **Maximum Improvement** – 75% to 99% improvement of the above-mentioned cardinal signs and symptoms.
- **Moderate Improvement** – 50% to 74% improvement of the above-mentioned cardinal signs and symptoms.
- **Mild Improvement** – 25% to 49% improvement of the above-mentioned cardinal signs and symptoms.
- **No Improvement** – Less than 25% improvement of the above-mentioned cardinal signs and symptom.

DEPARTMENTAL COLLABORATION

This study is being done at

1. PG Department of Shalya Tantra of Shri Krishna Govt. Ayurvedic College and Hospital, Kurukshetra
2. Research & Innovation Department; Shri Krishna Ayush University; Kurukshetra
3. Department of Microbiology, Kurukshetra University; Kurukshetra.

If required, cooperation of other departments of Shri Krishna Ayurvedic College and Hospital, Kurukshetra is being taken with due permission from concerned authority.

ETHICS AND DISSEMINATION –

Research ethical approval, after critical evaluation and presentation to the ethical committee, has been taken on the research topic No. CTRI/2022/08/044639

DECLARATION

- **Time Schedule:** This study is being completed within stipulated time limit.
- **Informed written consent:** Consent is being taken at time of registration.
- **Case Sheet:** Standard Case sheet has been prepared before starting the clinical trial.

DISSEMINATION POLICY

Will be in the form of paper publication, presentation and monograph.

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