



CLINICAL STUDY ON EFFICACY OF PRAPAUNDRIKADI GHRITA IN VRANA ROPANA WITH SPECIAL REFERENCE TO WOUND HEALING

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DOI: 10.48047/ecb/2023.12.si4.1611

ABSTRACT- A wound may be defined as the disruption of cellular and anatomical continuity of the soft part of body structures caused by violence or trauma. Healing of wounds is one of the important areas of clinical medicine explained in many Ayurveda texts under the heading "Vrana Ropana". *Vrana* and its management have been dealt with since the *Vedic period to the current era*. Thus, it is a major problem right from the early stages of medical study. Despite brilliant advancements in surgery, wound management is still a subject of speculation. The Present study consists of a Clinical Study of Prapaundrikadi Ghrita in patients of Suddha Vrana. This study is an interventional, randomized parallel group clinical trial with Ayurveda and Allopathic system intervention. In the present study, patients with clean wounds were registered from OPD/IPD of the Department of Shalya Tantra, Sir Sunder Lal Hospital BHU Varanasi, and were divided into two groups, Patients of both groups were cleaned & dressed daily & all the selected criteria were assessed on day 0,7,14 and 28 based on Bates Jensen Wound Assessment tool. *Prapaundrikadi Ghrita* is one of those formulations which is described in *Chakradutta*, *Bhaisajya Ratnawali*, and *Sushruta Samhita* for the management of the wound and abscess. The feedback data of the clinical trials and observations have been noted with the reduction in signs and symptoms according to the Bates Jensen wound assessment tool along with, the effect of the therapy and statistical analysis during the study.

Keywords- *BhaisajyaRatnawali*, *Chakradutta*, PrapaundrikadiGhrita, *Sushruta Samhita* Vrana, wound,

Introduction- Wound management is a multidisciplinary specialty taking numerous physiologic, immunologic processes as well as physical and social factors to achieve successful wound closure. Vrana and its operation have been dealt with since the Vedic period to the current period. Therefore, it's a major problem right from the early stages of medical study. In malignancy of brilliant advancements in surgery, wound operation is still a subject of enterprise.

The whole surgery revolves around the wound & no surgeon remains untouched by it. So, wound mending is a big hunt for all surgeons. A wound may be defined as the disruption of cellular and anatomical continuity of soft parts of body structures caused by violence or trauma. Healing of injuries is one of the important areas of clinical drugs explained in numerous Ayurveda textbooks under the heading "Vranaropana". Acharya Sushruta in Sushruta Samhita developed the same and also gave some further details about the wound and its mending. According to Sushruta, Vrana(wounds or ulcers) is the termination of the lining membrane that after healing leaves a scar for life. All living beings are bestowed with a natural miracle of form, rejuvenescence, and mending in due course of time. Still, wound mending is delayed and becomes delicate to manage if they come infected. A clean wound is an uninfected operative wound in which no inflammation is encountered and the respiratory, alimentary, genital, or uninfected urinary tract isn't entered. In addition, clean injuries are primarily closed and, if necessary, drained with unrestricted drainage. Operative incisional injuries that follow no piercing (blunt) trauma should be included in this order. (Bailey and Love's Short Practice of Surgery, 25th edition, Re-print 2008). In general, Infections caused by colorful pathogens are the most important factors responsible for detention in wound mending, accordingly leading to the conformation of a Dushta Vrana(habitual non-healing wound). Necrotic towels, bog, and foreign material in the wound can give a medium for infection and protract the seditious response which detainments mend. Necrotic towel and bog can be debrided by autolytic, natural, enzymatic, mechanical, and surgical means. Ancient Acharyas and ultramodern experimenters in this period both are having a single thing to achieve perfect health. Only because of this fact, enormous inquiries had been done into medical wisdom. From the actuality of life, there's a wound and there's a need for its operation. Proper wound care is necessary to help infection & to promote mending of the wound & fresh things if possible to have a good ornamental result after the wound has fully healed and this thing isn't yet fulfilled. As a great colonist of Ayurvedic surgery, Acharya Sushruta has also given equal significance to Vrana by giving the term ' Vrana Vinischayartham ' in the description of ShalyaTantra itself(Su.su.1/9).

The ulcer which is free from(the symptoms of) the three vitiated doshas, has bluish perimeters, granulation towel on position(of the skin face), and has no pain or discharge is said to be a clean one. That suggests the bottom(upper face) of the lingo, soft, wettish, smooth, effortless, good looking(indeed), and not percolating fluids are the features of suddhaVrana(pure/ unvitiated by doshas aseptic). Acharya Charak has also described the features of clean injuries in chapter 25th of Chikitsa Sthana. An ulcer that isn't veritably red, not veritably pale, not veritably brownish black, not associated with excruciating pain, not important elevated, and not associated with pockets (utsangi) is suitable for the administration of mending remedy. Sushruta also indicated the process by which impediments to Dushta vrana(habitual non-healing wound) can be removed therefore preparing the way for continued mending by a process known as ' VranaShodhana '. Once these impediments are removed normal mending process can be accelerated by the process described under the heading ' VranaRopana '(wound mending). therefore it can be said that Sushruta's operation of injuries was more thorough than the

operation of injuries present in this ultramodern period. Injuries in general and habitual non-mending/ Clean injuries, in particular, have been the subject of exploration for clinicians and croakers rehearsing colorful Pathies to find out cost-effective medicines and ways to cure similar injuries. In a country like India, where nearly 80 of the population resides in pastoral areas under poor aseptic and nutritive conditions, not only is the prevalence of delayed wound mending but they're also not suitable to go the treatment offered by the present interpreters. frequently due to their poverty and hygienic living conditions indeed simple injuries get infected to beget a great sufferance to them. Hence, there's a need to find out similar treatment modalities which are cheap, fluently available far and wide, and also free from side goods. In this environment, Ayurveda offers a shaft of a stopgap as it uses herbal medicines, frequently readily available in India, for curing injuries. One similar Ayurvedic expression, Prapaundrikadi Ghrita has been mentioned in Chakradutta(1) for its Vrana Ropana parcels by which it has been chosen for this study.

MATERIAL AND METHOD- The present study was planned to treat patients having wound of age ranging between 18 to 60 yrs. This study is an interventional, randomized parallel group clinical trial with Ayurveda and Allopathic system intervention. Before initiating this study, permission was obtained from the Institutional Ethics Committee of the institute; ECR/BHU/Inst/UP/Dean/2020/EC/2342 ,dated: 07/12/2020, and the study was also registered in CTRI(CTRI/2021/02/031344).

AIMS AND OBJECTIVE;The Present study consists of –

1. Clinical study of **Prapaundrikadi Ghrita** in patients of Suddha Vrana

Materials for the Study

A. Preparation of drug:

B. Dressing material: Surgical gloves, Tooth Forceps, Rough and Fine Scissors, Prapaundrikadi Ghrita, Normal Saline, Gauze, Cotton, and Bandage.

C. Wound Assessment

Ø **For Size Measurement:** Ruler, Pen, Notebook

Ø **Sequence Photography:** Digital Camera

Ø Cotton tipped applicator to assess Undermining

Ø Transparent metric measuring guide with concentric circles to determine the percent of wound involved.

The reason behind this research;

- I. The wound is a neglected area in surgery.
- II. Requires proper cleaning and dressing.
- III. The chance of infection is very high.
- IV. Lacking cost-effective treatment protocol.
- V. Decrease the burden on the patient and their relatives.
- VI. Health hazards due to negligence.
- VII. To minimize the duration of treatment.

VIII. No any previous work has been done on clean wounds and its healing in our department.

STUDY DESIGN–

This study is an interventional, randomized parallel group clinical trial with Ayurveda and Allopathic system intervention. (Wound healing activity of Ayurveda drug has been compared to allopathic drug). Before initiating this study, permission was obtained from the Institutional Ethics Committee of the institute; ECR/BHU/Inst/UP/Dean/2020/EC/2342, dated: 07/12/2020, and the study was also registered in CTRI(CTRI/2021/02/031344).

Collection of the Drug;

Raw materials (drugs) were collected from the local market in Varanasi, Uttar Pradesh.

Identification of raw samples (medicine):

The crude drugs were identified and authenticated by the Department of Botany, Institute of Science, BHU, Varanasi with voucher specimens as:

1. *Rubia cordifolia* Linn. (*Rubia*. 2021/1)
2. *Glycyrrhiza glabra* Linn. (*papilion*. 2021\14)
3. *Prunus cerasoides* D. Don (*Rosa*. 2021/1)
4. *Sacchrum officinarum* Linn. (*Poa*. 2021/5)
5. *Curcuma longa* Linn. (*Zingibera*. 2021/8)
6. *Vitiveriazinzanoides* (L) Nash. (*Poa*. 2021/6)

Methods of Study;

In the present study, 20 patients with clean wounds were registered from OPD/IPD of the Department of Shalya Tantra, Sir Sunder Lal Hospital BHU, Varanasi. Patients were registered irrespective of their age, sex, and religion; which are fulfilling the inclusion and exclusion criteria. Patients were enrolled after thorough interrogation, laboratory investigations, and clinical assessment on a well-set Performa. All the registered patients were randomly distributed into two groups; Group I (Trial Group) and Group II (Comparison Group). Criteria of Selection:

Inclusion Criteria

1. Clean wound
2. Diabetic Wound with Controlled Diabetes mellitus
3. Age between 18-60 yrs.

Exclusion criteria

1. Malignant Ulcer
2. Tubercular ulcer
3. Syphilitic ulcer
4. Ulcer in an uncontrolled diabetic patient.
5. HIV-positive patient
6. HBsAg, Anti-HCV positive patient
7. Patients who are suffering from chronic debilitating disease.
8. Who is not willing to give written informed consent

DISTRIBUTION OF PATIENTS

As per inclusion criteria, selected patients were registered for the study. They were randomly divided into two groups i.e. Group-I and Group-II.

Plan of Study

Present study was carried out on total of 20 patients with Clean wounds, were divided into 2 groups(Trial and comparison) of 10 patients each.

1. **Group I (Trial Group,10 patients)** – treated with Prapaundrikadi ghrita.
2. **Group II (Comparison Group,10 patients)** – treated with Placentrex gel.

In Group I (Trail Group) Local application of Prapaundrikadi Ghrita(prepared from six raw drugs) was applied on registered patients with clean wounds while in Group II (Comparison Group) patients with clean wounds were dressed(local application) daily with Placentrex gel.In both groups, Patients with clean wounds were dressed daily(application of drug)and all the selected criteria(10 out of 13 from the bates Jensen tool) were assessed on days 0,7,14, and 28.

Assessment Criteria – Bates Jensen Wound Assessment Tool

Investigations

Following Investigations were carried out in each registered patient.

CBC, Fasting Blood Sugar, post-prandial blood sugar, Blood Urea, Serum Creatinine, HIV, HBsAg, Anti-HCV

Statistical Methods

The data collected were transferred on master chart showing various items/variables in columns and subjects in rows, The analysis of data was done using statistical software IBM SPSS version 20.

The formula for mean and standard deviation are given below:

$$\text{Mean} = \frac{\sum x}{n} = \frac{\text{sum of the observations}}{\text{No.of observations}}$$

$$\text{Standard Deviation (S.D)} = \sqrt{\frac{\sum x^2 - \frac{(\sum x)^2}{n}}{n-1}}$$

‘X’ is the mean value ‘n’ is the number of observations

Chi-square test –

This test has been applied to test the significance of difference between proportion of day 0 (before treatment) and day 14 (3rd follow up, after treatment), Whenever excluded frequency is less than 5 then this test has been calculated after suitable proportions in the rows or columns.

$$\chi^2 = \sum \frac{(O - E)^2}{E}$$

O = Observed Frequency

E = Exposed Frequency

P = is the proportional occurrence of observed value by chance.

Cut off value is 0.05

Level of Significance –

P value: Less than 0.05 has been taken as statistically significance

P value: Less than 0.01 is highly significance

P value: Greater than 0.05 is not significant

Paired 't' test was applied to test the significance of mean of difference of paired observations (within the group / intra group comparison)

$$t = \frac{\text{Mean of difference}}{\text{S.E of difference}}$$

In the present study intra group, comparison was done at base line (day 0) and the end of trial (day 28) and for between the group comparisons separately comparing means at Day 0 and Day 28 was done. When the observed data do not satisfy the assumptions test then corresponding non-parametric test may be applied or data transformation may be done. Nonparametric test corresponding to paired 't' test is Wilcoxon Signed Ranks Test and McNemar Test.

For intra group (within the group) comparison at Registration Vs Follow up Wilcoxon Signed Ranks Test and McNemar Test has been applied. Pearson chi-square test was used for intergroup comparison.

Result and discussion

According to the observation and result discussed above few conclusions can be drawn;

i. The size of the wound was decreased(on comparison)in both the groups but on observing the data(statistical) it concluded that Prapaundrikadi ghrita is better than Placentrex gel when it comes to the effect in decreasing the size of the wound.

ii. Depth of the wound was decreased(on comparison)in both the groups but on observing the data(statistical) it concluded that Prapaundrikadi Ghrita is better than Placentrex gel when it comes to the effect in decreasing the Depth of the wound.

iii. The edge of the wound was decreased(distinct to indistinct, diffuse, even with wound base)in both the groups but on observing the data (statistical) it concluded that Prapaundrikadi ghrita is less effective than Placentrex gel in the healing of edges.

iv. The exudate type of the wound was decreased (from serosanguineous to bloody and none)in both the groups but on observing the data(statistical) it concluded that Prapaundrikadi ghrita is better than Placentrex gel.

v. Exudate amount of the wound was decreased (from large to moderate to scanty) in both the groups but on observing the data(statistical) it concluded that Prapaundrikadi ghrita is less effective than Placentrex gel.

vi. Skin color surrounding the wound was improved(from non-blanchable to blanchable)in both the groups but on observing the data(statistical) it concluded that Prapaundrikadi Ghrita is better than Placentrex gel.

vii. Peripheral tissue edema near the wound was decreased(from pitting to non-pitting to absent)in both the groups but on observing the data(statistical) it concluded that Prapaundrikadi Ghrita is less effective.

viii. Peripheral tissue induration near the wound was decreased (from 2 - 4 cm to <2 cm around the wound)in both the groups but on observing the data(statistical) it concluded that Prapaundrikadi Ghrita is better than Placentrex gel.

ix. There was a significant improvement in Granulation tissue in both groups but on observing the data(statistical) it concluded that *Prapaundrikadi Ghrita* is less effective than Placentrex gel.

x. There was a significant improvement in Epithelialization of the wound in both groups but on observing the data (statistical) it concluded that *Prapaundrikadi Ghrita* is less effective than Placentrex gel.

DISCUSSION

Major findings of the study:

Exudates: Clinical study showed that there was a reduction in the number of exudates during regular follow-ups in all groups. Statistical analysis showed that between these groups reduction in exudates was noted but the difference is non-significant. This analysis reveals that *Prapaundrikadi Ghrita* is effective in terms of reduction in exudates type of wound as compared to Placentrex gel. This is probably due to some qualities of *Prapaundrikadi Ghrita* such as *ruksha guna*, *kashaya rasa* and *tikta rasa*. These qualities help to reduce the amount of exudates from wounds.

The bark of sugarcane (*Sacchrum officinarum*)⁸⁻⁹ demonstrates a strong antibacterial activity on gram-negative bacteria indicating its high antibacterial potential and effectiveness in the treatment of wound infection that's the reason behind the healing of wounds in Group I without getting again infected by. Its flavonoid has been reported to possess anti-inflammatory activity it also possesses antioxidant activity.

Extract of *Rubia cardifolia*¹⁰ shows marked infiltration of the inflammatory cells, it increases the blood vessel formation and enhanced proliferation of cells resulting in rapid healing of wounds treated with *Prapaundrikadi Ghrita*, this drug prevents the prolongation of the inflammatory phase resulting in decreased healing time, tannins and anthraquinone are major phytoconstituent present in this plant which may be required for wound healing, it also has an antibacterial effect along with anti-inflammatory effect.

*Glycyrrhizha glabra*¹¹⁻¹²-Its aqueous extract of leaves possesses the ability of wound healing by decreasing the level of wound area resulting in a decrease in the size of the wound thereby increasing the percentage of wound contraction and decreasing pus discharge (decreasing Exudate amount). It is also active against some bacteria like *E.coli*, *staphylococcus aureus*, and *Pseudomonas fluorescens* which commonly infect the clean wound again and again if precautions are not made.

*Prunus cerasoides*¹⁴- Its phytoconstituent shows the activity of antipyretic, antioxidant, anti-inflammatory, and analgesics. Some studies revealed that it contains antimicrobial activity against both gram-positive as well as gram-negative bacteria which avoids further contamination of wounds.

*Curcuma longa*¹⁵⁻¹⁷-This plant is having an active ingredient which is curcumin having an analgesic and anti-inflammatory effect, it contains vitamins A, B, and C which have an important role in the healing of wounds and regeneration of cells. Turmeric ends in the early synthesis of collagen fiber by mimicking fibroblast activity. It also acts as an antioxidant as free radicals are considered to be the major cause of inflammation during the wound healing process. Curcumin application on wounds enhances epithelial regeneration and increases fibroblast proliferation and vascular density thereby increasing cutaneous wound healing through involvement in tissue

remodeling granulation tissue formation and collagen deposition. So we can conclude that the reduction in exudates in wounds by application of *Prapaundrikadi Ghrita* is because of the synergistic action of all six individual drugs having anti-inflammatory and anti-microbial action.

Probable mode of Action Of Drug:

On the basis of results of clinical study probable mode of action of trial drug i.e *Prapaundrikadi Ghrita* on clean wound can be postulated hypothetically. As already discussed, *Prapaundrikadi Ghrita* possess properties like *kashaya and tikta rasa, sheeta virya, ruksha and laghu guna*. Classically prepared *Prapaundrikadi Ghrita* showed good result in decreasing the size, depth, exudate type, improving the skin color surrounding wound area, and decreasing the tissue induration.

1) Rasa –

a) ***Kashaya Rasa***: Excessive reactionary inflammation in wound is inhibited due to its *Kashaya rasa*. In the earlier phase, *Kashaya rasa* expels out toxins and necrotic tissues, it also reduces the local discharge and irritation. By this way drug reduces excessive exudation and thus granulation tissue formation is facilitated which is necessary for wound healing.

b) ***Tikta Rasa***: *Tikta rasa* has good debridement properties. It is also a good wound-cleansing agent which reduces local exudates and pus and thus helps to balance the moisture of the wound.

2) ***Sheeta Virya***: *Sheeta virya* has anti-inflammatory action. It also helps to stop accidental bleeding during debridement. *Sheeta virya* provides nutrition to newly forming tissue in wound bed. It also relieves a burning sensation in the wound.

3) Guna:

a) ***Ruksha*** : This also acts as an anti-inflammatory and effective debridement property. It also reduced local discharge and irritation.

b) ***Guru***: *Guru guna* of drug facilitates wound tissue epithelization and proliferation .It also provides nutrition to newer forming cells of wound. This *guna* also alleviates vitiated *vata* and thus helps to reduce symptoms produced due to vitiated *vata* and thus helps to reduce symptoms produced due to vitiated *vata*-like pain.

4) ***Prapaundrikadi Ghrita*** is a formulation having 6 raw drugs with the characteristics of *Vrana shodhana* and *Vrana Ropana*.

a) ***Prapaundrikadi Ghrita*** possess all property of *Vrana shodhana* and *Vrana ropana* like *katu, tikta and kashaya rasa* which helps in the Cleaning of wound(*shodhana* of *Vrana*) whereas *madhura, tikta and kashaya rasa* helps in healing of wound(*Vrana ropana*) like *ruksha, sheeta, tikta rasa, Kashaya rasa* etc.

b) These types of drugs have tendency to reduce size, depth, type of exudates of wound, Colour of skin surrounding the wound and peripheral tissue induration.

Limitations of study:

To access the *Shodhana* property of this drug.

To evaluate the possibility of using *Prapaundrikadi Ghrita* in clean as well as in chronically infected wounds.

Sample Size : No. of patients i.e., 20 is a very small size. The main problem in small sample sizes is small sample difference which is significantly more likely to be spurious than large samples.

The process of wound healing is a dynamic process that includes cellular and biochemical changes which vary in different phases of wound healing. From the present study, it is clear that the trial drug Prapaundrikadi Ghrita shows almost equal effect in the healing of wounds compared to the standard drug Placentrex gel, and this trial drug is found to be more cost-effective than Placentrex gel.

Prapaundrikadi Ghrita is highly effective in treating wounds as there was a significant reduction in exudates and peri-wound area and helps in the formation of healthy granulation tissue of wound as observed during the clinical study. The healing property of *Prapaundrikadi Ghrita* can be seen in the significant reduction of wound contraction and faster unit healing time.

The possibilities of the mechanism of action of Prapaundrikadi Ghrita described on the basis of phytochemicals are as:

FLAVONOID- Anti-oxidant, anti-inflammatory, analgesic

PHYTOSTEROL- Antioxidant, antibacterial, anti-inflammatory.

TANNIN- Anti-oxidant, anti-inflammatory, analgesic, increases collagen content, styptics

TERPENOIDS –Antioxidant, antibacterial, anti-inflammatory, antifungal

SAPONINS – Anti-oxidant, anti-inflammatory, antimicrobial.

Therefore, this compound shows a significant effect on wound healing (Vrana Ropana)

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