EVALUATION OF EFFICACY OF DASHMOOLARISHTA IN CERVICITIS: A PROOF-OF-CONCEPT STUDY

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ABSTRACT

Dashamoolarishta, a well known polyherbal formulation used for different ailments especially for inflammation and need clinical validation of its efficacy in cervicitis which is important but neglected disorder. Present research work was carried out with the aim to evaluate the efficacy of Dashamoolarishta on cervicitis. Study was conducted in perimenopausal patients to assess the efficacy of trial drug “Dashamoolarishta”. Total of 30 perimenopausal patients were selected for the study after screening 113 patients. Out of them, 30 patients completed the study. The trial drug Dashamoolarishta was given in the dose of 20 ml BD for 90 days with water and follow up was conducted after every 15 days. The study revealed the statistically significant decrease in cervical redness, swelling, low backache. Significant inflammatory changes were observed in pap smear test. ESR was significantly decreased after treatment. Dashamoolarishta is a potential drug for cervicitis.

Key words: Dashamoolarishta, efficacy, Cervicitis.

INTRODUCTION

Cervicitis is an inflammation of the uterine cervix, most often caused by infection. However, in a few cases it may be attributed to chemical exposure or a foreign body, such as a pessary (a device inserted into the vagina to support the uterus), cervical cap (a birth control device), or diaphragm. The condition may also be caused by an allergy to contraceptive spermicides
or to latex in condoms.\textsuperscript{[1]} In cases of cervicitis attributed to foreign objects, infection is still frequently the cause, but the presence of the foreign object may make the cervix more susceptible to infection.\textsuperscript{[2]}

There is increasing evidence that \textit{Mycoplasma genitalium} and \textit{Chlamydia trachomatis} causes mucopurulent cervicitis and endometritis in women.\textsuperscript{[3,4]} Sexual partners of \textit{M. genitalium} and \textit{C. trachomatis} infected patients harbour the pathogens of genital tract which are ultimately responsible for cervicitis as well as urethritis.\textsuperscript{[5]} There are evidences that other causes of cervicitis may include infections with herpes virus (genital herpes), \textit{Ureaplasma urealyticum, Candida} spp., \textit{Staphylococcus epidermidis, Lactobacillus} and \textit{Staphylococcus aureus}.\textsuperscript{[3,6,7]} Along with this some other determinants of cervicitis may include persistent abnormalities of the vaginal flora, idiopathic inflammation, altered local host immune response etc.

The symptoms of cervicitis include abnormal vaginal discharge, cervical bleeding, cervical ectopy, elevated vaginal PMNL (polymorpho-nuclear leukocytes) count and vaginal pain. Also there are evidences that many times it is asymptomatic.\textsuperscript{[3]} Generally antibiotic or antifungal therapies either orally or per vagina are prescribed to treat this condition. Many times exogenous hormonal therapies are suggested so as to increase the local immune response against pathogens.\textsuperscript{[6]} For local tissue destruction in case of chronic cervicitis with ectropion available treatment options are cryotherapy, electrocauterization, laser therapy, cold conization or loop diathermy.\textsuperscript{[8]} Although these medicines are well tolerated by majority of the patients and there are no major adverse effects, the search is always going on to explore more effective medicine.

\textit{Ayurveda} considers that all gynecological disorders are caused by vitiation of \textit{vata dosha}. While treating \textit{vata dosha}, the drug of choice is \textit{Dashamoola}. \textit{Dashamoola} contains \textit{Brihatpanchamoola} and \textit{Laghuspanchamoola}. All plants of \textit{Brihatpanchamoola} have \textit{tikta}, \textit{khashaya rasa}, \textit{ushna veerya} and \textit{katu vipaka}, whereas the constituent plants of \textit{Laghuspanchamoola} have \textit{khashaya}, \textit{tikta rasa}, \textit{ushna veerya} and \textit{madhura vipaka}.

\textit{Dashmoola} is mentioned under \textit{Shothahara} (anti-inflammatory) (Ch./su./4/16, 38) and \textit{Vata hara} drugs (Ch./su./3/19). The type of formulation (\textit{Arishta}) is known to reach small channels and act with immediate effects. Further, these plants are reported to have anti-inflammatory, anti-fungal and wound healing properties.\textsuperscript{[9,10]} Individually root extracts of various plants of \textit{Dashamoola} viz. \textit{A. marmelos},\textsuperscript{[11]} \textit{P. integrifolia},\textsuperscript{[12]} \textit{D. gangeticum},\textsuperscript{[13-16]} \textit{O. indicum}\textsuperscript{[17,18]} and
U. picta,\textsuperscript{[19]} S. suaveolen\textsuperscript{[20]} have exhibited anti-inflammatory potential in vivo. Also in a comparative study of roots of Dashamoola plants it has shown that all plants as well as Dashamoola as a whole possess wide-ranging in vivo anti-inflammatory potential.\textsuperscript{[21a\&b]} Dashamoola is also known for having antimicrobial activity.\textsuperscript{[9]}

Dashamoolarishta, a well known drug prepared from Dashamoola is traditionally used as an analgesic as well as anti-arthritic agent. It is used for cough, rheumatism etc. and also suggested for ovulation related disorders.\textsuperscript{[22,23]} Dashamoolarishta have shown to posses anti-inflammatory activity in cotton pellet induced granuloma and carrageenan induced rat paw edema models.\textsuperscript{[24]} Also it is shown that Dashamoolarishta has peripheral as well as central analgesic activity in various animal models.\textsuperscript{[24,25]} In a study it is shown that Dashamoolarishta possess highest anti-inflammatory potential amongst selected dosage forms of Dashamoola in carrageenan induced rat paw edema model.\textsuperscript{[21a]}

In our previous work we have studied different market samples of Dashamoolarishta for their free radical scavenging as well as anti-inflammatory activity and it was found that Dashamoolarishta samples have exhibited significant anti-oxidant and anti-inflammatory activity.\textsuperscript{[26]} Several studies have carried out to validate the potential of Dashamoola churna and individual plants of Dashamoola but no study has been carried out to evaluate the efficacy of Dashamoolarishta. With this background, the present study was undertaken to evaluate efficacy of Dashmoolarishta in patients suffering from cervicitis.

**Aim and Objective**

To evaluate the efficacy of Dashamoolarishta in cervicitis as an anti-inflammatory agent.

**Type of study**

Open clinical trial

**MATERIALS AND METHODS**

**Preparation of formulation**

Dashamoolarishta was prepared as per the standard procedures mentioned in Ayurvedic Formulary of India (AFI).\textsuperscript{[27]}

**Selection of cases**

Total 48 perimenopausal patients (age group 40-60 years) were selected from 113 patients for the present study after screening 113 patients at Bharati Ayurved Hospital. Out of them 30
patients completed the study. The study procedures were initiated after obtaining Written Informed Consent from each patient.

**Dose and duration**

The trial drug “Dashamoolarishta” was given in the standard dose of 20 ml BD for the period of 90 days with water and follow up was conducted after every 15 days.

**Inclusion criteria**

- Female patient of age group 40-60 years i.e. perimenopausal.
- Indoor, outdoor patient suffering from cervicitis.

**Exclusion criteria**

- Age group of menarche.
- Pregnant ladies
- Cervical polyp patients
- Patients with any malignant growth of genitalia
- Any other chronic disability related with cervix

**Adverse effect evaluation criteria**

Possible adverse effects of test drug ‘Dashamoolarishta’ were recorded during every followup from patients in the form of information like change in appetite, sleep, drowsiness, nausea, vomiting, pain in abdomen, stool & urine related complaints (Mala and Mutra) and other non specific symptoms.

**Assessment criteria**

Selected patients were assessed using general assessment criteria before and after the treatment. At the baseline, a detail history with emphasis on the gynecological and obstetric details was taken from all patients. Physical and systemic examination was carried out. All the patients were evaluated for signs and symptoms using subjective as well as objective parameters.

**Subjective parameters**

- Cervix: Redness, Swelling, Vaginal discharge, Presence of tenderness, hardness & pain was assessed using gradation method as shown in Table 1
- General symptoms: Low backache and Menstrual disorders
Table 1: Gradation of parameters

<table>
<thead>
<tr>
<th>Grade</th>
<th>Redness</th>
<th>Swelling</th>
<th>Discharge</th>
<th>Tenderness</th>
<th>Pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>White/Normal colour</td>
<td>Normal tissues</td>
<td>No complaint of white discharge</td>
<td>No pain</td>
<td>No pain</td>
</tr>
<tr>
<td>1</td>
<td>Pink</td>
<td>Granulation tissue complete</td>
<td>Vaginal and vulvar moistness</td>
<td>Tenderness on touching cervix</td>
<td>Pain while work</td>
</tr>
<tr>
<td>2</td>
<td>Red</td>
<td>Inflammation</td>
<td>Severe quantity : needs pad</td>
<td>Tenderness on mobilization of cervix</td>
<td>Pain felt while work and rest and needs painkiller</td>
</tr>
<tr>
<td>3</td>
<td>Deep red</td>
<td>Erosion and inflammation</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Tenderness of the Cervix: graded as Normal, Soft like lips and Hard, Swelling when there is feeling different from lips

Objective parameters
- Blood parameters (VDRL, HIV, Haemogram – Hb%, TLC, DLC, ESR)
- Urine Routine and Microscope

Other parameters
Age, Weight, Prakruti, Parity, Abortions, Mode of Delivery, Mutra, Mala and Yoni-vyapada

The patients were screened for VDRL and HIV tests to rule out the concerned diseases. They were also investigated for Pap smear tests, blood parameters like Hb%, TLC, DLC, ESR and urine routine and microscopy examination.

Follow-up and monitoring
All registered patients were called for follow up after every 15 days for the period of 90 days. During followup, patients were observed for signs and symptoms of cervicitis.

Ethical clearance
The present work was reviewed and discussed by Institutional Ethics Committee and has been approved on 09 April 2012 (Letter no-F10 (5)/EC/2012/292).

Assessment of results and progress
The data of the clinical study was analyzed after the treatment for the effect on cervical redness, swelling, vaginal discharge, presence of tenderness, hardness & pain.
Statistical Analysis
The data are expressed as Median (Range). Pre and Post treatment values were analyzed using Wilcoxon Rank Sum Test. p<0.05 was considered as level for significance. All analysis was done using Graphpad Instat Version 3.

OBSERVATION AND RESULTS
Over a period of 08 months, 113 names of patients with low back pain as their main complaint were referred to the study. Out of these, 48 patients were included in the study. Total 18 patients were drop out from the study due to their discontinuation of treatment. The remaining 30 patients were investigated for the study.

The mean age of recruited patients was 52.23 ± 4.79 years. Prakriti evaluation of these patients showed almost equi-distribution of all 3 prakriti types (9 patients each of Kapha and Vata prakriti and 12 patients of Pitta prakriti). Out the 30 patients, 1 patient was nulliparous, 4 were primi para and 25 were multi-para. 26 patients gave history of normal delivery and 4 patients had LACS. In 23 patients, there was no history of abortion where as single abortion reported in 6 patients and multiple abortions in 1 patient. 21 patients gave history of abdominal surgery, while 16 patients gave history of Urinary Tract Infection. There was history of ano-rectal conditions like piles and fissures in 10 patients.

Effect of Dashmoolarishta on signs and symptoms of cervicitis:
The signs and symptoms of cervicitis were evaluated pre and post treatment using the scores as described in materials and methodology. The results are summarized in Table 2.

Table 2: Effect of Dashmoolarishta on signs and symptoms of cervicitis

<table>
<thead>
<tr>
<th>Signs/symptoms</th>
<th>Pre-treatment</th>
<th>Post-treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical Tenderness</td>
<td>1 (0-2)</td>
<td>0.5 (0-2)***</td>
</tr>
<tr>
<td>Redness of Cervix</td>
<td>1 (0-2)</td>
<td>0 (0-2)***</td>
</tr>
<tr>
<td>Swelling of cervix</td>
<td>1 (0-2)</td>
<td>0 (0-1) ***</td>
</tr>
<tr>
<td>Low backache</td>
<td>1 (0-2)</td>
<td>0 (0-1) ***</td>
</tr>
</tbody>
</table>

Data expressed as Median (Range), (**p<0.001) using Wilcoxon Rank Sum Test as compared to Pre-treatment values
All the parameters showed significant decrease after administration of Dashmoolarishta. Cervical tenderness that was graded as normal and hard did not show any change post treatment.

**Effect of Dashmoolarishta on Pap smear**

29 patients showed inflammatory changes in Pap smear pre-treatment, which was changed to mild inflammatory changes in 4 patients and no inflammatory changes in 15 patients. In 10 patients no change was seen. These changes were statistically significant when analysed using Chi square test (p<0.001).

**Effect of Dashmoolarishta on blood parameters:**

Total leucocyte count and ESR was estimated in all patients in both pre and post treatment and which ESR showed significant decrease after administration of Dashmoolarishta.

**Table 3: Effect of Dashmoolarishta on blood parameters**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pre-treatment</th>
<th>Post- treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>TLC (/cu.mm)</td>
<td>8900 (4800-14100)</td>
<td>8300 (5200-14200)</td>
</tr>
<tr>
<td>ESR (mm/hr)</td>
<td>19 (7-40)</td>
<td>16 (5-30)***</td>
</tr>
</tbody>
</table>

Data expressed as Median (Range), (***p<0.001) using Wilcoxon Rank Sum Test as compared to Pre-treatment values.

**DISCUSSION**

In the present study, we evaluated the efficacy of Dashmoolarishta in cervicitis. *Dashmoolarishta* is recommended to treat inflammation of joints. It is also used in various gynecological conditions and even in post-partum peruid. There are anecdotal reports available on its use in cervicitis.[22,23] However, no clinical studies have been found in literature evaluating its efficacy in cervicitis.

An open, non-comparative study was carried out in 30 patients. We observed higher prevalence of cervicitis in multi-para females, those with history of normal delivery and in the patients who had Urinary Tract Infection in the past indicating associaiation of these factors with the development of cervicitis. Interestingly, there were 10 patients with history of ano-rectal conditions like piles and fissures highlighting role of pre-existing *Apan vayu dushti* mentioned in Ayurveda as an important causative factor.
Dashmoolarishta when given in a dose of 20 ml BD for a period of 90 days showed significant improvement in all the signs and symptoms. It also significantly improved inflammatory changes observed in vaginal smear. The total leukocyte count showed reduction as compared to baseline and ESR reduced significantly indicating resolution of the underlined infection.

In support of these results, some of the Dashamoola plants have been examined for their anti-inflammatory potential viz. A. marmelos,\textsuperscript{[11,28]} P. integifolia,\textsuperscript{[12]} D. gangeticum,\textsuperscript{[13-15,16]} O. indicum,\textsuperscript{[17,18]} U. picta,\textsuperscript{[19]} S. suaveolens.\textsuperscript{[20]} Also there are reports on antimicrobial activity of some of the Dashamoola plants viz. Tribulus terrestris,\textsuperscript{[29,30]} Premna serratifolia,\textsuperscript{[31]} Solanum xanthocarpum.\textsuperscript{[32]} Along with these Dashamoola as a whole also exhibited anti-microbial activity against some bacteria and fungi.\textsuperscript{[9]} These reports advice that the obtained activity of Dashamoolarishta in present study is might be due to anti-inflammatory as well as anti-microbial activity of ingredient plants of Dashamoola.

Similar studies are reported on different herbal formulations. In an open clinical trial, women suffering from vaginitis and cervicitis were suggested for topical application of V-Gel (a polyherbal formulation) on the vagina and cervix. Reduced soreness of cervix, pruritus, inflammation of vulva, vaginal discharge within two weeks of drug treatment suggested that V-Gel was clinically effective formulation for the treatment of vaginitis and cervicitis.\textsuperscript{[33]} Another clinical study conducted on a famous Unani formulation, Marham Dakhlion has shown that it is effective on chronic cervicitis and cervical erosion. Study has shown that the formulation was effective in 80\% of the cases.\textsuperscript{[34]}

These studies are in concorded with the present investigation and revealed that Dashamoolarishta is exhibiting anti-inflammatory activity against cervicitis. This study however has some limitations. Since it was an open study with no comparator especially in view of the subjective nature of parameters, it did not completely rule out bias on the part of the investigator and placebo response on the part of the patients. Inclusion of microbiological outcomes assessing the clinical isolates from Pap smear could be used for future studies of this kind in addition to inflammatory markers specific to cervicitis. Our findings further open up new avenue to test the formulation for cervicitis with respect to cytological as well as molecular changes.
CONCLUSIONS
Thus, our study reports the efficacy of *Dashmoolarishta* in cervicitis for first time without any adverse effect.

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REFERENCES
2. Falk L, Fredlund H, Jensen JS. Signs and symptoms of urethritis and cervicitis among women with or without *Mycoplasma genitalium* or *Chlamydia trachomatis* infection. Sex Transm Infect, 2005; 8:73-78.


