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Effect of Lucronil® Tablets in the Patients with Leucorrhea: An Open Clinical Trial

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Abstract: ***Leucorrhoea is a common gynaecological problem causing discomfort and disturbance in day to day activities of women. In view of unavailability of specific treatment to manage the condition, we evaluated efficacy and safety of Tab. Lucronil® on the clinical signs and symptoms of Leucorrhea. After obtaining Ethics Committee permission and written informed consent, a total of 31 patients were recruited in the study. These patients were asked about the color, odor, consistency and degree of vaginal discharge before and after the treatment. Cervical smear was also collected to assess inflammatory changes. Tab. Lucronil® was administered as two tablets (500 mg) twice a day after meals with water for a period of one month. We observed that Tab. Lucronil® reduced the symptoms of Leucorrhoea in 8 patients within the duration of 15 days. The remaining 23 patients showed significant reduction ($p < 0.001$) in the degree of cervical discharge and inflammation ($p<0.01$). There were no adverse effects reported during the study period. Tab. Lucronil® was well tolerated by all the patients as evident from the good compliance. Our study thus highlights the efficacy and safety of Tab. Lucronil in leucorrhoea.***

Keywords: Lucronil Leucorrhea

1. Introduction

Poor genital hygiene in Indian women has been responsible for high prevalence of excessive vaginal discharge[1]. Leucorrhoea, one of the most common manifestations of gynecological disorders, is an important psychosomatic disorder affecting the psychology of women irrespective of socio-economical status and occupation[2]. The symptoms of leucorrhoea include discharge, backache, weakness, frequent micturition, constipation, anorexia, headache and dragging sensation in abdomen[3]. Excessive vaginal discharge is most often seen in women of reproductive age group. It can be due to vaginitis with inflammation of vaginal mucosa caused by Trichomonas vaginalis or yeast like fungus Candida[4]. Although there is a high prevalence of infective pathology involved in Leucorrhea, studies report that about 93% of the females had inflammatory smears when evaluated for Pap smear[5].

The treatment of this manifestation, although virtually depends on its etiopathology, invites immediate measures. Further, till date no definite solution is available to treat the problem.

Hence the present study has been planned to evaluate efficacy and safety of Tab. Lucronil® in the clinical signs and symptoms of Leucorrhea due to inflammatory pathology as evaluated by the Pap smear examination. Lucronil® is an Ayurvedic proprietary medicine containing 11 herbs, 1 insect gall and 1 ingredient of mineral origin. It is expected that Tab. Lucronil® will provide various benefits viz. relieve infections, boost immunity, maintain hormonal levels and thereby alleviate white discharge or prevent its recurrence.

2. Materials and Methods

Study design: Phase II Clinical Trial
The study was an Open label prospective Clinical study.

Objectives
The primary objective of the study was to evaluate the efficacy of Tab. Lucronil® on clinical signs and symptoms of leucorrhoea and Pap smear findings and also to evaluate the tolerability of Tab. Lucronil® clinically in patients suffering from leucorrhoea.

Investigational product
Tab Lucronil® is an Ayurvedic proprietary medicine containing the following ingredients Ashwagandha Extract (*Withania somnifera*) 40 mg, Vidari kanda Extract (*Pueraria tuberosa*) 20 mg, Badi Elaichi Extract (*Amomum subulatum*)30 mg, Ashok Chhal Extract (*Saraca indica*)40 mg, Lodhra Chhal Extract (*Symplocos racemosa*)60 mg, Haldi Extract (*Curcuma longa*)40 mg, Chirayta Extract (*Swertia chirata*)30 mg, Vasa Extract (*Adathoda vasica*) 30 mg, Bilwa Extract (*Aegle marmelos*)30 mg, Guduchi Extract (*Tinospora cordifolia*) 30 mg, Majufal Extract (*Quercus infectoria*)20 mg, Shatavari (*Asparagus* racemiosus) 30 mg, Dugdhapashan (Silicate of Manganese) 30 mg.

Ethical Considerations
The study was initiated after obtaining Institutional Ethics Committee permission (BVDUCOA/EC/765 A). Written Informed Consent was obtained from the patients before performance of any study related procedures. The study was conducted in accordance with the ethical principles of declaration of Helsinki. The study has been registered under the Clinical Trials Registry of India (CTRI/2015/02/005515).

Patients screening and Recruitment
Females (age group, 20- 45 years) with complaints of white discharge attending the Out Patient Department of Bharati Ayurved Hospital, Department of Prasutitantra and Stree Rog fulfilling the eligibility criteria were recruited in the study.

Inclusion criteria
Married non- pregnant and non-lactating females aged 20 to 45 years were included in the study. The patients with leucorrhoea due to non-infective cervical lesions e.g. cervical erosion, chronic cervicitis, mucous polyps, increased pelvic congestion e.g. uterine prolapse, acquired

retroverted uterus, chronic pelvic inflammation were included in the study.

Exclusion criteria

Patients on Oral Contraceptive Pills, with Intrauterine Contraceptive Device (IUCD), with physiological leucorrhoea (e.g. during ovulation, pre-menstrual, during pregnancy), abnormal (excessive) vaginal discharge due to neoplasmic changes, women with positive history of venereal diseases, patients suffering from uncontrolled diabetes and women with Hemoglobin percentage below 7 gm % were excluded from the study.

Dosage

Tab. Lucronil® was administered as two tablets (500 mg) twice a day after meals with water for a period of one month.

Study Procedure

The study was initiated after obtaining Institutional Ethics Committee permission. The patients fulfilling the eligibility criteria were recruited in the study. Written Informed Consent was obtained from the patients before conducting any study related procedures.

At the baseline visit, all patients underwent routine Hematological investigations (Hb, CBC and ESR), Random Blood Sugar, VDRL, HIV and Urine routine and microscopy. Further a thorough per vaginal examination was carried out to assess presence / absence of erosion and to examination of the cervical discharge in terms of color (watery/white/creamish white/yellowish white), odor (present/absent), consistency (sticky, curdy & and purulent) and degree of vaginal discharge (mild, moderate and severe). Cervical smear was also collected.

All the patients were administered Tab. Lucronil® in the dose two tablets twice a day after meals with water for a period of one month. Patients were asked to visit the hospital after 15 days to evaluate any adverse event and concomitant medicine usage during the study period. Per vaginal examination was done, if necessary as per the clinician's advice. Per vaginal examination and Pap smear were repeated after the completion of treatment to evaluate the efficacy of Tab. Lucronil®.

Tolerability assessment

The tolerability was assessed in terms of any unwanted effects after the consumption of Tab. Lucronil® such as nausea; vomiting, loose motions etc. were assessed during the follow up visits.

Statistical Analysis

Chi-Square test (or Fisher's exact test as applicable) was applied to find out the difference between the number of patients demonstrating a particular sign or symptom pre and post treatment.

3. Observation and Results:

A total of 91 patients with chief complaint of white discharge were screened for the study, of which only 43 patients were recruited. Out of these 43 patients, 2 patients failed the screening process and hence were excluded from the study. Thus, 41 patients were administered study drug, of which 31 patients completed the study. 7 patients lost to follow up, 2 patients were non- compliant and 1 patient was withdrawn as per investigator's discretion and was shifted to modern medication.

The average age of the 31 recruited patients was 32.45 ± 6.61 years. The mean Hemoglobin % (Hb in gm %) of the patients was 11.71 ± 1.84 and the mean Random blood sugar (RBS in mg) was 90.51 ± 13.60.

Ultrasonography (USG), VDRL (Venereal Disease Research Laboratory) Test and Human immunodeficiency virus (HIV) test were done to rule out neoplasm, infective pathology and HIV respectively. The baseline USG findings in the patients are shown in Table 1.

Table 1: Baseline USG findings in completed patients (n=31)

USG Findings	*Number of patients*
No abnormality	17
Pelvic Inflammatory disease (PID)	6
Polycystic Ovarian Syndrome (PCOS)	2
Simple Ovarian cyst	1
Bulky uterus	1
Bulky uterus with PID	1
Marginally bulky uterus with tiny nebothian cyst in cervix	1
Marginally bulky uterus, Simple ovarian cyst	1
Small right Ovarian dermoid	1

No abnormality was detected in 17 patients while 1 patient was reported to have a simple ovarian cyst, 2 patients had bulky uterus, 1 of them had associated PID (Pelvic Inflammatory disease), 2 patients had marginally bulky uterus, of them 1 patient had nebothian cyst in the cervix and 1 patient reported of simple ovarian cyst. 6 patients reported signs of PID, 1 patient reported a small right ovarian dermoid and 2 patients reported of PCOS (Poly-Cystic Ovarian Syndrome). VDRL Test was found to be negative and HIV test was non- reactive in all the recruited patients.

Of the 31 patients who completed the study, 8 patients got relief from symptoms within 15 days of administration of the medicine. In these patients the Pap smear and per vaginal examination could not be done at the end of the study due to relief in symptoms. Hence, these patients could not be considered for statistical evaluation in absence of post-treatment values.

The data of the remaining 23 patients has been reported. Cervical examination was done in all the patients' pre and post. 15 patients had healthy cervix, 5 patients had Grade I erosion and 3 patients Grade II erosion. At the end of the study, 17 patients had healthy cervix, 1 patient had cervical redness and 5 patients had Grade I erosion.

The color of the cervical discharge was assessed before the initiation of the study and after the completion of the study. Initially, 21 patients had white color discharge, while 1 patient had creamish white and 1 patient had yellowish white discharge. After the completion of the study, 1 patient

had watery discharge, 4 patients had whitish discharge and 18 patients had white colored discharge.
In all the patients, there was absence of foul smell of the discharge before the initiation of the study and after the completion of the study.

The consistency of the cervical discharge before the initiation of the study and after the completion of the study was assessed. 22 patients had sticky discharge and 1 patient had curdy discharge in the beginning of the study. After the completion of the study, 2 patients had watery discharge and 21 patients had sticky discharge. None of the patients had curdy discharge at the end of the study.

The degree of discharge was graded as absent, mild, moderate and severe. At the initiation of study, 19 patients had mild discharge, while 1 had moderate and 3 patients had severe discharge. After the administration of study drug for 30 days (after completion of study) 20 patients had absence of discharge, 2 had mild discharge, 1 patient had moderate discharge and no patient had severe discharge. The difference between pre and post treatment was statistically significant.. The same has been depicted in Table 2.

Table 2: Effect of Tab. Lucronil on Degree of cervical discharge (n=23)

Degree of discharge	*Number of patients*	
	Pre	*Post*
Absent	0	20
Mild	19	2
Moderate	1	1
Severe	3	0

$p < 0.0001$ using Fisher's exact test

Pap smear of the patients was investigated before the initiation of the study and after the completion of the study. 17 patients reported of inflammatory smears, while 6 patients reported no inflammation at the initiation of the study. After completion of the study , out of 17 patients 12 patients reported relief from Inflammation. The results were statistically significant. The same has been depicted in Table 3.

Table 3: Effect of Tab. Lucronil on Inflammation (n=23)

Inflammation	*Number of patients*	
	Pre	*Post*
Present	17	5
Absent	6	18

$P < .01$ using Fisher's exact test

Tab. Lucronil® was well tolerated by the patients as there were no untoward effects reported by any of the patients.

4. Discussion

In the present study we evaluated the effect of Tab. Lucronil® a herbomineral formulation in patients of Leucorrhoea. A total of 31 patients were administered Tab. Lucronil®. We observed that Tab. Lucronil® reduced the symptoms of Leucorrhoea in 8 patients within the duration of 15 days. In remaining 23 patients who completed 30 days of treatment showed significant reduction ($p < 0.0001$) in the degree of cervical discharge and inflammation ($p < .01$) . The other symptoms also showed improvement. The findings highlight the efficacy of Tab. Lucronil in leucorrhoea.

There were no adverse effects reported during the study period. Tab. Lucronil® was well tolerated by all the patients as evident from the good compliance.

Shweta pradara (Leucorrhea) in the classical texts is not considered as a disease but as a predormal symptom in many of the gynecological diseases. *Kapha dosha* is considered as the major cause for the painless, excessive vaginal discharge [6].

The formulation contains 11plants extract, 1 insect gall and 1 ingredient of mineral origin. 5 plants possess *Kashaya*, *Tikta Rasa* & 2 plants possess *Katu*, *Tikta* combination, while 2 each of *Madhura* and *Katu Rasa.* 8 plants have *Katu Vipaka* and 4 plants have *Madhura Vipaka*. 7 plants possess *Sheeta veerya* and 5 *Ushna Veerya*. Based on these pharmacological attributes the activity of the formulation can be assessed. *Katu*, *Tikta*, *Kashaya Rasa*[7], the *Katu Vipaka*[8] and *Ushna Veerya*[9] are mainly responsible for pacifying *Kapha*. The significant decrease in the degree of discharge may be attributed to these properties. The *Kashaya Rasa* is mainly responsible for the *Stambhana karma* which is responsible for the decrease in the discharge; the *Tikta Rasa* helps in cleansing the *Kapha dosha* and helps maintain the equilibrium of the Kapha dosha.

The *Madhura Rasa*, *Madhura Vipaka* and *Sheeta Veerya* dravya mainly help in the *Balya* and *Brimhana karma* and hence provide strength to the reproductive organs. They also act as rejuvenators.

Leucorrhea is mainly caused due to inflammation of the pelvic organs, due to bacterial and fungal infections and low immunity. The ingredients of the formulation have individually reported to possess immunomodulatory properties, antibacterial properties and utreotonic properties.

Ashwagandha is reported to possess immunomodulatory activities. It is also found to enhance total white blood cell count, delayed type hypersensitivity reaction and to enhance phagocytic activity of macrophages[10]. *Ashoka* reports uterotonic and antibacterial properties [11]. The extract of Lodhra bark at two different doses showed promising improvement in treating female reproductive dysfunctions induced by cold restraint stress. The extract also significantly suppresses inflammation[13].

Clinical Studies have shown that the alkaloid vasicine present in *Vasa* has significant uterotonic activity. This action appears to be influenced by the presence or absence of certain estrogens[14]. Significant antibacterial activity against the Gram-positive bacteria strains Streptococcus faecalis, Staphylococcus aureus, Staph epidermidis and the gram-negative E. coli were also noted[15].

Bilwa is reported as an anti-inflammatory agent in both acute and chronic models of inflammation[16].The antimicrobial activity of chloroform, methanol and water extract was performed by disc diffusion method. There was significant antibacterial activity of the leaves, fruits and

barks of Bilwa[17]. Vidari kanda is also proved to be a potent scavenging agent for ABTS radical cation in a concentration dependent manner, showing the direct role in trapping free radicals[18].

Ela fruit aqueous extract in a dose of 100mg/ml and 200mg/ml exhibited anti-inflammatory activity against Carrageenan induced paw edema in rats[19]. The secondary metabolites such as flavonoids, triterpinoids present in Chirayata play a significant role in anti-inflammatory, anti microbial and antioxidant properties of this plant[20].The aqueous extract of Guduchi are reported to possess antioxidant properties[21].

Shatavari, in spite of being a rejuvenating herb is beneficial in female infertility, as it increases libido, cures inflammation of sexual organs and even moistens dry tissues of the sexual organs and normalizes the uterus and the changing hormones [22].
Haridra extract and the essential oil inhibit the growth of a variety of bacteria, parasites, and pathogenic fungi. Oral administration of curcumin in instances of acute inflammation was found to be as effective as cortisone or phenylbutazone, and one-half as effective in cases of chronic inflammation[23].

The galls of the plant *Quercus infectoria* possess therapeutic activities, with particular efficacy against inflammatory diseases. Oral administration of extract from the plant has been reported to significantly inhibit prostaglandin E2 (PGE2)[24].

The formulation is thus found to possess all the properties essential for the management of Leucorrhoea. In the present study also the formulation is found to be effective in the management of Leucorrhoea caused due to pelvic inflammatory diseases and is well tolerated by patients.

However the study has certain limitations. The study has been conducted without control. The microbiological evaluation of the smear could not be done due to limited resources. This provides scope for further research, where studies can be conducted in the patients of infective pathology as most of the ingredients of the formulation possess antibacterial properties.

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