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Evaluation of *Majoon Ushba* in Cervicitis – A Randomized Standard Controlled Single Blind Study.

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Abstract

Objectives: To evaluate the efficacy and safety of *Majoon Ushba* and Tablet Doxycycline in Cervicitis.

Material and Methods: A randomized standard controlled single blind study was carried out in the Department of Gynecology at the National Institute of Unani Medicine. Clinically diagnosed patients (n=45) were randomized to the test (n=30) and control (n=15) groups by computer generated random table No. The inclusion criteria were married patients aged 18 to 40 years with symptoms of vaginal discharge, lower abdominal pain, low backache, dysuria, dyspareunia, pruritus vulvae and post coital bleeding. The exclusion criteria were unmarried, pregnant or lactating women, patients with pelvic pathology or malignancy using oral or intrauterine contraceptive devices, sexually transmitted diseases and concomitant diseases. In the test Group, *Majoon Ushba* was given 10 gm BD orally after menses for 15 days for 3 consecutive cycles. In control group, Tablet Doxycycline 100 mg BD was given orally after menses for 7 days for 3 consecutive cycles. The results were analyzed by Kruskal-Wallis with Dunn's multiple comparison, Wilcoxan match pair, Mann Whitney test, Student t' test, Fisher's exact test and Chi-square test.

Results: There was a significant improvement in the subjective and objective parameters in both test and control group. The test drug was found to show more response than the control in the management of cervicitis with p value<0.05

Conclusion: The test drug was found to be useful and effective in the management of cervicitis. Further, the effectiveness should be evaluated in large sample size with recent techniques.

Key words: Majoon *Ushba;* cervicitis; Centre for disease Control

Introduction:

Women represent over half of the population and use more than 50% of health care resources. Gynaecological health is an important component of any women's health status. Gynecological disorders can have a substantial impact on many aspects of quality of life, including reproductive ability, sexual functioning, mental health and the ability to work and perform routine physical activities.[1-3] Cervicitis is defined as inflammation of the columnar epithelium of the endocervix or inflammatory process in cervical epithelium and stroma or infection of the endocervix including stroma and glands.[4-7] Clinically presence of yellow or green purulent exudates, more than 10 white blood cells per high power field (hpf) on cervical gram staining, ectopy of cervix with erythema, edema and friability.[8,9] Chronic inflammation of the cervix is very common and is seen in about 35-85% of women. It is usually a histological diagnosis. It is found in nearly all multiparous and nulliparous, cervices.[7,10] Acute cervicitis occurs after trauma due to parturition or abortion, inappropriate use of tampons or infection by pathogenic agents like streptococcus, staphylococcus, E. coli, Neisseria gonorrhoea, Chlamydia trachomatis.[10-12] Approximately, one-third of all women with vaginal discharge have cervicitis. The Centre for Disease Control (CDC) and prevention estimates that over 19 million STIs occur annually, almost half of them among aged 15-24 years. The etiology of infective cervicitis is variable and consists commonly of STIs.[5, 9,13]

In *Unani* system of medicine, the concept of humoral theory was first proposed by *Hippocrates* in 460 BC. He stated that if *Akhlat arba* (morbid humours) are in a state of equilibrium, both qualitatively and quantitatively health is restored. Any derangement in these humours either qualitatively or quantitatively leads to disease.[14] According to the Humoral theory, it is *dam* (blood), *safra* (bile) or occasionally *sauda* (black bile) or *balgham* (black bile) which are involved and dominant in *warme unqur rehm* (cervicitis). Hence the abnormal accumulation of morbid humours causes *Sue Mizaj* (deranged temperament) of uterus leading to cervicitis. The therapeutic options for cervicitis in conventional medicine include antiseptics, antibiotics, ablation by cryosurgery, electro diathermy, Co2 laser, cold coagulation and surgical interventions like trachelorrhapy, cone biopsy, trachelectomy and hysterectomy.[15] The surgical procedures cannot be availed by the poor sections of population. Looking at the side effects of conventional therapy and complications of surgical procedures, it is need of the hour to switch to an alternative system of

medicine that is safe, cost effective, nonsurgical and can be easily availed by everyone with long lasting effects. Though the treatment of this disease dates back to ancient period, but validation and documentation are extremely deficient. Keeping the above facts in view, the present study was undertaken to evaluate the efficacy and safety of the *Unani* drug in the management of *Warme unqur rehm* and to compare the results of *Unani* herbal drug with standard drugs in controlled manner.

MATERIAL AND METHODS

Design: A prospective, single center, randomized standard controlled, single blind, pre and post evaluation study was conducted in the Outpatient department of Amraze Niswan (Gynecology) at the National Institute of Unani Medicine, during the year 2010-2011. This study was started after the approval from institutional ethical committee. The intervention was given for 3 consecutive cycles.

Participants: A total number of 98 patients were screened for cervicitis during the study period. Fifty five patients were subjected to preliminary investigations and out of them ten patients were excluded (4 PCOS, 2 Pregnant, 1 DM, 2 Ovarian cysts, Fibroid).

The written consent was obtained from the patients, who fulfilled the inclusion criteria. They were evaluated through the complete history and physical examination. The inclusion criteria were married women aged 18 to 40 years with symptoms like white discharge, low backache, low abdominal discomfort, dyspareunia, postcoital bleeding, vulval itching, and dysmenorrhoea. The exclusion criteria were unmarried, pregnant or lactating women, patients with pelvic pathology and carcinoma, using oral or intrauterine contraceptive devices, with any concomitant diseases like hypertension, diabetes mellitus, and sexually transmitted diseases. The pelvic examination was performed to evaluate the cervicitis-related signs like vaginal discharge, bleed on touch, and to note the state of cervix, its position, direction, consistency, irregularity, or any other abnormalities. The subjective parameters like WDPV, LBA, LAP, pruritus vulvae and dysuria and the objective parameters like hypertrophy and congestion of cervix were assessed by grading system [15,16.] Similarly, dyspareunia, post coital bleeding and foul smell, nabothian follicles and bleeds on touch were assessed by the presence or absence.[15, 16]

Investigations: The baseline clinical laboratory investigations such as haemoglobin percentage, total leucocytes count, differential leucocytes count, erythrocyte sedimentation rate, VDRL and Random blood sugar were done to exclude general diseases. Ultrasonography and Papinicoulaou smear were done to exclude the pelvic pathology and malignancy. Cervical swab and culture for culture and sensitivity was done to see the organism involved. To assess the safety of drugs, blood urea, serum creatinine, SGOT, SGPT, and Alkaline phosphatase were done before and after trial. At every follow up of 15 days during three months of study period, progression or regression of symptoms and signs were recorded in the case record form.

Intervention: The patients were randomly allocated to the test (n=30) and control Groups (n=15) by computer generated table No. In the test Group, 10 gm BD *Majoon Ushba* was given orally after menses (3 consecutive cycles). The control Group received orally, Tab Doxycycline 100gm BD for 7 days after menses (3 consecutive cycles).[17]

Outcome: The outcome measures were to assess effectiveness of trial drugs on subjective and objective parameters. The patients each in the test and the control Group were assessed on day one before starting the treatment and after administration of the test drugs or the standard control for 3 consecutive cycles. The cervicitis was considered cured when there is complete resolution of signs and symptoms, improved when there was incomplete resolution of signs and symptoms where as not cured, when there was no apparent response or worsening of signs and symptoms after treatment.[18]

Statistical Analysis: The results were analyzed statistically using Graph Pad Instat version 3.00 for window (Graph Pad Software, San Diego, Calif, USA) at the completion of the study taking in account the relief of symptoms and healing of the erosion. Results on continuous measurements were presented on Mean (Median) and results on categorical measurements were presented in Number (%). Significance was assessed at 5 % with 95% confidence interval. Subjective parameters were analysed by implying Kruskal-Wallis with Dunn‘s multiple comparisons test (both intra and inter group comparison) while as objective parameters were assessed by Kruskal- Wallis with Dunn‘s multiple comparisons and Fisher‘s exact (2-tailed) test (both inter and intra group comparison). The safety evaluation was done by Mann Whitney U (two-tailed, independant), Wilcoxan match pair test and Student‘t‘ test (2-tailed, paired & unpaired) for inter and intra group comparison. The overall efficacy of test drug and control drugs were assessed by Chi-square test.

OBSERVATIONS AND RESULTS

The Socio-demographic (literacy status, socioeconomic status, parity, age at marriage) characteristics and investigations of the test and control groups are shown in Table 1. It was found that the parameters were statistically not significant. ($P > 0.05$) Thus, the groups were homogenous in terms of biochemical parameter and age before intervention. (Table 1)

Table -1: Socio-demographic Characteristics of Test and control groups

Characteristics	**No. of Patients**	
	Test Group n=30	**Control Group** n=15
Age (years) Range		
	25-40	22-40
Literacy status		
Illiterate		
Primary School	07	03
Middle School	13	04
High School	0	0
Intermediate	0	02
Graduate or Above	08	04
Socioeconomic Status	02	02
Upper		
Upper Middle	02	0
Lower Middle	10	08
Upper Lower	08	03
Lower	09	04
Parity	01	0
Nulliparous		
1	0	01
2	01	01
3	10	04
>4	13	04
Age of Marriage	06	05
<20 years		
20-24	22	8
Cytological Patterns	08	12
Mild Inflammatory		
Moderate Inflammatory	17	
Severe Inflammatory	12	07
	01	08
		0

Test used: Unpaired _t' test for investigations, P > 0.05, considered not significant, Data are

shown as Mean ± SD and number (percentage)

Efficacy of the Test Drug and Control on Objective Parameters

The data was statistically analysed using Kruskal-Wallis test with Dunn's Multiple comparison test and Fisher's Exact test. The median rating score after treatment in the test group when compared with median rating score before treatment in control and median rating score after treatment in control was found to be significantly reduced (P < 0.05). (Table 2)

Table-2: Efficacy of Test Drug and Control on Objective parameters

Objective Parameters	**Test group(n=30)**			**Control group(n=15)**		
	BT Mean(median)	**AT Mean(median)**	**P value**	**BT Mean(median)**	**AT Mean(median)**	**P value**
Hypertrophy	2.56(3)	1.36(1)	<0.001***	2.46(3)	1.73(1)	NS
Congestion	2.6(3)	1.36(1)	<0.001***	2.6(3)	1.6(2)	<0.01**
Discharge	1.63(2)	1.06(1)	<0.001***	1.33(1)	1.21(1)	NS
Cervical swab culture	6	2	NS	2	2	NS

***** Highly significant <0.001 **Quite significant <0.01**

*** Significant <0.05 NS Not significant <0.05**

Test used: Kruskal-Wallis test with Dunn's Multiple comparison and Fisher's exact (two tailed)

test (for both inter and intra group). Although the inter group comparison is not significant (P value >0.05)

Effect of Test Drug and Control on Subjective Parameters

The most common symptom in the present study was white discharge. The median rating score for white discharge and other symptoms are in the test group after treatment [0(0, 0)] was significantly reduced (P < 0.001) when compared to median rating score with range before treatment of the test and control group. The median rating score of other symptoms are summarized. (Table 3)

Table-3: Efficacy of Test drug and Control on Subjective parameters of Cervicitis

Symptoms (subjective parameters	Test group(n=30)			Control group(n=15)		
	BT Mean(median)	AT Mean(median)	P value	BT Mean(median)	AT Mean(median)	P value
WDPV	2.8(3)	1.4(1)	<0.001***	2.86(3)	1.93(2)	<0.5*
Abnormal vaginal odour	1.63(2)	1.23(1)	<0.005*	1.73(2)	1.26(1)	NS
LBA	4.66(4)	2.86(2)	<0.001***	4.13(4)	2.8(2)	<0.005*
LAP	3.4(4)	2.66(2)	<0.005*	2.53(2)	2.26(2)	NS
Dyspareunia	1.63(2)	1.2(1)	<0.01**	1.73(2)	1.33(1)	NS
Dysuria	2.2(2)	1.26(1)	<0.001***	2.33(2)	1.6(1)	<0.5*
Post coital Bleeding	1.3(1)	1.1(1)	NS	1.4(1)	1.26(1)	NS
Pruritis vulvae	2(2)	1.23(1)	<0.001***	2(2)	1.13(1)	<0.01**

*** Highly significant <0.001 ** Quite significant <0.01

* Significant <0.05 NS Not significant <0.05

Test used: Kruskal-Wallis test with Dunn's Multiple comparison test (for both inter and intra

group). Although the inter group comparison is not significant (P value >0.05)

Therapeutic Outcome

In the test Group, out of 30 patients of cervicitis, 16 (53.33%) patients were cured completely and in the control Group 4(26.66%) patients were cured. The data was analysed by Chi-square test and the comparison revealed that the difference in the cure was significant (P =0.2347). (Table 4)

Table -4: Therapeutic Outcome of Test Drug and Control on cervicitis

Therapeutic response	Test (n=30)	Control (n=15)
Cured	16(53.33%)	4(26.66%)
Improved	6(20%)	5(33.33%)
Not cured	8(26.66%)	6(40%)

Chi square test used, Degrees of freedom=2, P value= 0. 2347

DISCUSSION

This study demonstrates that the test drug was effective in the management of cervicitis. The laboratory investigations were within normal range before and after treatment showing that the drug was safe. Till date, none of the studies in the Unani system of medicine had evaluated or documented the efficacy and safety of the test drug in the management of cervicitis. Thus, it is difficult to correlate the finding with other clinical studies but it validates the claim made by the Unani Scholars. According to the Unani Scholars, *Warme unqur rehm* is caused by *Ufunat* (infection) and

it needs *dafe tafun* (antimicrobial) and *mohallil* (anti-inflammatory) drugs to relieve infections and associated symptoms like vulval itching, dysuria, postcoital bleeding. Moreover, these drugs are used for healing the wound and ulcers since they are having *Musaffie Khoon* (blood purifier), *Musakkin* (analgesic), *Qabiz* (astringent) and *Mundamile qurooh (*wound healing) properties.Hence, it is assumed that the properties of the test drug has caused relief in the sign and symptoms of cervicitis

Effect of Test Drug and Control on Subjective Parameters

The most common symptom in the present study was white discharge. The mean and median for WDPV in test group before and after treatment was statistically significant with P value <0.001 when compared to mean and median before and after treatment in control group. This improvement may be due to *qabiz, mujaffif, mohallil, dafe taffun, musaffie khoon* properties of *ushba* . This result coincides with the findings as documented by *Ibn Baitar*,[19] *Kabeerrudin*,[20] *Ghani*,[21] *Roy* [22] *Gayathri*.[23]

The mean and median for foul smell in test group before and after treatment was statistically significant with P value <0.001 when compared to mean and median before and after treatment in the control group. This improvement may be due to *dafe taffun, mujaffif and musaffie khoon* properties of *ushba*. This result coincides with the findings as documented by *Ghani*[21]and *Gayathri*.[23]

The mean and median for pruritus vulvae in test group before and after treatment was significantly reduced with P value <0.00 when compared to mean and median before and after treatment in control group. This improvement may be due to the *musaffie khoon*, *qabiz* properties of *ushba.* This result coincides with the findings as documented by *Ibn Baitar* [19]and *Roy*[22]

According to VAS score used for assessment of LBA, the mean and median in test group before and after treatment was statistically significant with P value <0.001 when compared to mean and median before and after treatment in control group. The improvement may be due to the *mohallil* and *musakkin* properties of the ushba. This result coincides with the findings as documented by *Ibn Baitar*, [19]*Kabeerrudin*,[20] *Ghani* [21] and *Roy*.[22]

According to VAS score used for assessment of LAP, the mean and median in test group before and after treatment was 3.4(4) and 2.66(2) respectively. It was statistically significant wit P value <0.05 (Kruskal-Wallis with Dunn‘s multiple comparison test) compared to mean and median before and after treatment 2.53(2) and 2.26(2) in control group. The improvement was due to the *mohallil* and *musakkin* properties of *ushba* . This result coincides with the findings documented by *Ibn Baitar*, [19] *Kabeerrudin*,[20]*Ghani*, [21]*Roy* [22] and *Gayathri.*[23]

The mean and median for dysuria in test group before and after treatment was statistically significant with P value <0.001 when compared to mean and median before and after treatment in control group. This improvement may be due to *mudire boul* effect of *ushba*. This result coincides with the findings documented by *Ghani*[21]and *Roy*.[22]

The Mean and median for dyspareunia in test group before and after treatment was statistically significant with P value <0.001 when compared to mean and median before and after treatment in control group. This improvement may be due to the *musakkin* properties of the *ushba*. This result coincides with the findings documented by *Ibn Baitar*[19]and *Kabeerrudin*.[20]

The mean and median for post coital bleeding in test group before and after treatment was statistically not significant with P value >0 as compared to mean and median before and after treatment in control group. This improvement may be due to the qabiz, *dafe qurooh* and *mujaffif* properties of the *ushba*. This result coincides with the findings documented by *Ibn Baitar* [19] and *Kabeerrudin*.[20]

Effect of Test Drug and Control on Objective Parameters

The mean and median for congestion of cervix in test group before and after treatment was statistically significant with P value <0.001 as compared to mean and median before and after treatment in control group. This improvement may be due to the *mohallil, dafe taffun* properties of the *ushba*. This result coincides with the findings documented by *Ibn Baitar*,[19] *Kabeerrudin*,[20]*Ghani* [21]and *Gayathri*.[23]

The mean and median for hypertrophy in test group before and after treatment was statistically significant with P value <0.001 as compared to the mean and median before and after treatment in control group. This improvement may be due to the *mohallil* properties of the *ushba*. This result coincides with the findings documented by *Ibn Baitar*,[19] *Kabeerrudin*,[20] *Ghani*[22]and *Gayathri.*[23]It was observed that 3 out of 6 patients after treatment showed cervical swab negative in test group with P value =1.00 (Fisher‘s Exact test, two-tailed) with 95% CI=0.3093=5.44.All the patients show inflammatory changes in the Pap smear (24-mild, 20-moderate, 1-severe inflammatory smear). Furthermore, It has been Pharmacologically proven that *Ushba* [21]is having antimicrobial and anti-inflammatory property that have inhibited the growth of organism and decreased the inflammation respectively. This finding was well correlated with the study conducted by Parsons WL and Wilson et al who found that inflammatory changes on cytology are associated with cervical infection.[26]The patients were followed up for three months after completion of the trial of the disease to observe the recurrence. However, no recurrence of this disease was found in the patients who got relieved completely of symptoms and signs of cervicitis except of three patients (1 in test and 2 in control). Moreover, though the response was seen in 53.33% patients, it is appreciable since, antibiotics and antiseptics have limited response in conventional medicine. Further studies with large sample size, double blinding and modified recent techniques are recommended.

CONCLUSION

The cervicitis is considered as a potential risk factor for sexually transmitted diseases. It is a major public health problem. In addition, the symptoms related to cervicitis have substantial impact on many aspects of quality of life, including reproductive ability, sexual functioning, mental health

and the ability to work and perform routine physical activities. Therefore, it must be treated with due care. This study proves that *Unani* herbal drug was found to be safe and effective in the management of cervicitis when compared to the standard. The study also validated the claim of the *Unani* physicians in the treatment of cervicitis.

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Conflict of Interest: The authors whose names are listed certify that they have NO affiliations or any financial interest in the subject matter or materials discussed in this manuscript.

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