Research Article

A prospective, single arm study: To evaluate the efficacy of Majun kundur in the management of Stress urinary incontinence

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Abstract:
Purpose- Stress urinary incontinence common in women of all ages, and billions of dollars are spent each year to correct the condition and improve quality of life. It is today's need to explore the treatment option through traditional medicine system. Considering this, the study was carried out to evaluate the efficacy and safety of *Majun kundur* in stress urinary incontinence.
Material & Methods: This was a prospective, open-label, single-arm clinical study with women who have SUI to compared efficacy of *Majun kundur* before and after treatment. All patients (n=30) received *Majun kundur* 5gm with water twice a day for 8 weeks.
The primary outcome measure was change in subjective parameter i.e. International Consultation on Incontinence Questionnaire Urinary Incontinence Short Form (ICIQ-UI SF), and secondary outcome measure was change in objective parameters i.e. stress test and PERFECT score.
Results: SUI is significantly improved after intervention. There is strongly significant improvement in ICIQ score i.e. 13.80±2.30 before and 3.20±2.62 after the intervention with P<0.001. PERFECT score has shown highly significant change before and after the treatment with P<0.001. Stress test was positive in 30(100%) of patients before intervention, where as it was positive in only 3(10%) after intervention which is more significant with P<0.0001.
Conclusion: Test drug provide statistically highly significant improvement in stress urinary incontinence. It can be the alternative treatment for SUI. Further research in large sample size is advisable with prolongation of intervention.
Key words: *Majune kundur,* PERFECT score, Quality of life, *Salas al-bawl*, Stress test, Stress urinary incontinence

Asian Journal of Complementary and Alterantive Medicine.
Volume 05, Issue 16
Published on: 20/08/2017.
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Cite this article as: Fazly Shakoor, Wajeeha begum, Iram Naaz, Misba Naim. *Activities of Photo Activated Cow Urine Administration on Some Hematological Profile in Adult Male Wistar Rats.* Asian Journal of Complementary and Alterantive Medicine, Vol 5(16):1-6, 2017.

INTRODUCTION

Stress urinary incontinence(SUI) is the uncontrolled loss of urine on exertion e.g. coughing, laughing, sneezing.[1,2] According to the World Health Organization, urinary incontinence is a "wide spread global disease and one of the last medical taboos to many people."[3,4]

SUI accounting for 50% of all types of incontinence and this is the major type of incontinence in young and middle-aged women.[5] More than 200 million people worldwide suffered from SUI, and affects more women than men with an approximate ratio of 3:1.[6]

Urine leakage occurs when the pressure in the bladder and expulsive force is greater than the pressure within the urethra, i.e. closure force. Incontinence also occurs if there is a malfunction of the urethral sphincter or weakness in the pelvic floor muscles that support the bladder and other pelvic organs. Pregnancy and childbirth, especially by vaginal delivery,[7,8] nerve injuries to the lower back and pelvic surgery are also potential risk factors for the development of SUI because they weaken the pelvic floor muscles.[7] An increased BMI, smoking, chronic cough, diabetes, depression, and constipation are other conditions that can contribute to incontinence.[2,7,8]

In classical *unani* text urinary incontinence defined under the term of *salas al-bawl* and it is defined as involuntary loss of urine or unable to control urine. In the opinion of unani scholars, *salas al-bawl* is the

symptom of various diseases and also described the causes and treatment in detail. The causes that mentioned are *su'-i-mizaj barid*(abnormal cold temperament), *istirkha al-mathana* or *istirkha-e adala al-mathana(*flaccidity of urinary bladder muscles), excessive use of *mudirrat* (diuretics), *sue-mizaj har* (abnormal alteration of warm temperament), *khal 'al-faqrat-i-mathana* (damage to supporting structures of urinary bladder), excessive pressure on *matahna* by the gravid uterus, excessive *sufl* in stomach, *warm* (inflammation) in surrounding organs etc are the risk factors. *Humudat-i-bawl*(burning micturition), *sang-i-mathana (*bladder stone*)*, *khal al-mathana* (displacement) etc. and diabetes, intestinal worms in children *khuruj-al-maq'ad* (rectal-prolapse), *tukhma*(indigestion),*falij*(paralysis), injury to spinal cord also leads to incontinence. *Salas al bawl* should be treated according to cause like if the cause is *burudat wa rutubat* and *istirkha* then treat with *har wa qabid advia.* If cause is *hararat* then treat with *advia mubarrida wa munqabida,* likewise it can be treated by *Ilaj bi'l ghidha' (*diet*)*, *Ilaj bi'l dawa (*medicine), *Ilaj bi'l tadbir (*regimental therapy*).* [9,10,11]

Though SUI is not life-threatening but is a condition that can diminish the QoL of sufferers. Sufferers tend to be more depressed, experience higher levels of anxiety and feel more stigmatized compared to women who are not incontinent.

Over the last few decades' interest in the incorporation of patient assessed health status or quality of life (QoL) measure into the evaluation of the management of urinary incontinence has increased. Consequently the success of treatment can no longer be judged on clinical parameters alone and quality of life needs to be considered in both clinical and research settings. There are many validated questionnaires available and these questionnaires categorized as generic and disease or condition specific.[12]

By considering above mentioned fact it is important to diagnose and treat SUI as early as possible. Treatment options for SUI include strengthening the pelvic floor muscles with exercise, pharmacotherapy, and several surgical methods.[13] More than 200 surgical procedures have been described in literature and these procedures have veered between the overly simplistic (anterior colporrhaphy, needle suspensions) and the extremely complicated (traditional sub urethral slings).[1,14] Many studies have reported that conservative treatments can be helpful in managing SUI, with consensus groups recommending PFMT as the first-line treatment but PFMT is time consuming and requires high levels of motivation and a willingness to carry out an intense training programme. Modern drug therapy and surgical method also have their own health hazards.[1]

Therefore it is today's need to explore the treatment option through traditional medicine system.

Unani system of medicine has a great healing art as well as science. It treats a person as a whole not as a group of individual parts. It is aimed at treating body, mind and soul. India has accepted it as one of the alternative health care system and has given it official status. The World Health Organization (WHO) has also recognized the Unani System of Medicine (USM) as an alternative system to cater the health care needs of human population.[15] In view of this it is the need of the present era to evaluate the efficacy of unani drugs because unani literature enriched with many single drugs and compound formulations which can be used to treat the SUI. And also USM are easily accessible, cheaper and relatively safer than other conventional medicines. Considering all these facts it has been decided to conduct a clinical trial to evaluate the efficacy of *Majune kundur* in the management of SUI.[16,17]

METHODS

This was a prospective, open-label, single-arm, single centre study with women who have SUI. The study was approved by the Ethics Committee of national institute of unani medicine, (IEC No.-NIUM/2014-2015/010/ANQ/02) and was performed in National institute of medicine (NIUM) Hospital, Bengaluru during a time period of 2015 to 2017.

Patients: Inclusion criteria were the parous women aged between 20 to 60 years with symptoms of SUI as evidenced by provocative stress test, whereas women with known systemic diseases like diabetes mellitus, uncontrolled hypertension, and bronchial asthma and known malignancies and patients with continuous leakage of urine, enuresis, any pelvic pathology, genitourinary fistula, with history of surgery for stress urinary incontinence within 6 months, pregnant and lactating women were excluded from the study.

30 women with symptoms of SUI with positive stress test were enrolled in this clinical trial, after being completely explained about study conditions and

signing informed consent. Enrolled women instructed to take *Majun kundur* 5 gm. twice daily for 8 weeks. Research drug provided by pharmaceutical department of NIUM, Bengaluru.

Each subject had an enrolment visit and four follow-up visits at 2nd, 4th, 6th, 8th week and one after treatment follow up visit at 12th week after admission. At first visit after assessment of eligibility, baseline data (including age, weight, BMI, *mizaj*, education, parity, mode of delivery) level were collected, Appropriate investigations like hemogram, CUE, urine culture & sensitivity, LFT, RFT,RBS and USG whole abdomen was done and each participant was provided with the study medication and instructions on use.

Clinical outcome measures and procedure: Subjective parameter was (ICIQ-SF)[18] Objective parameters were Provocative Stress test[19] and PERFECT method.[20] The primary objective was to evaluate the efficacy and safety of *Majun kundur* in subjective improvement of SUI symptoms. The secondary objective was to assess the efficacy of *Majun kundur* in improving the objective parameters of SUI. At each follow-up visit, data about use of the study product and evaluation of ICIQ-SF and PERFECT score and about adverse events were collected. At the 8th and final visit at 12th week, with above mentioned data provocative stress test also performed. The investigator team contacted each subject by telephone for follow-up visits to ask about continued use of the product, and to ensure that the subject had sufficient supply to last until the next scheduled visit.

Statistics: Data was analysed By SAS 9.2, SPSS 15.0,Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1. Mean±SD were used to calculate categorical and continuous measurements respectively. Student t test (two tailed, dependent) has been used to find the significance of study. P ≤0.05 was considered statistically significant.

RESULT

Patients (n=62) of SUI were assessed for eligibility, among which 10 patients denied to participate in study, 52 patients were accepted for enrollment. Out of 52, 22 patients were excluded for not meeting the inclusion criteria; 30 patients who fulfilled the inclusion criteria were enrolled in the study (Fig.1) Patients demographic and baseline characteristics are presented in in (table 1).For ICIQ-UI short form score Mean±SD before and after treatment 13.80±2.30 and 3.20±2.62 with p-value <0.001(table2) shows strongly significant improvement.

Changes in PERFECT-score: Mean±SD of P(power) before and after treatment was 2.27±0.78, 3.70±0.47 respectively and P-value is <0.001, Mean±SD of E(endurance) before and after treatment was 4.53±1.07 and 7.00±0.98 respectively with P-value of <0.001, Mean±SD of R(repetition) before and after treatment was 4.20±0.85 and 6.57±0.97 respectively and P-value was <0.001. Mean±SD of F(Fast) before and after treatment was 4.77±0.77 and 6.83±1.02 respectively with P-value was < 0.001 (table 2) and for Stress test Mean±SD before and after treatment 1.00±0.0, 0.00±0.00 respectively with P value of <0.0001 (table 2). No adverse effects were reported with regard to test drug consumption.

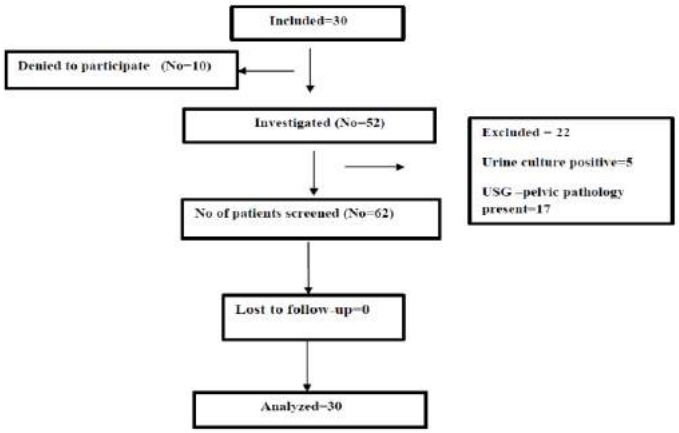

Figure 1. Participant flow chart

Demographic data	% of patients	Mean ± SD
Age (years)		
30-40	46.7	42.67±8.21
41-50	36.7	
51-60	16.7	
Occupation		
Unemployed	73.3	-
Skilled worker	13.3	
Semi-skilled worker	10.0	
Unskilled worker	3.3	
Mizaj		
Balghami	66.7	-
Saudawi	13.3	
Damwi	10.0	
Safrawi	10.0	
BMI (kg/m²)		
<18.5	0.0	26.25±2.10
18.5-25	26.6	
25-30	66.7	
>30	6.7	
Menstrual status		
Menstruating	66.7	-
Post-menopausal	30.0	
Hysterectomised	3.3	
Parity		
1	10	2.8±1.095
2	33.3	
3	30	
4	20	
5	6.7	
Mode of delivery		
FTND	80%	
LSCS	10%	
Both	10%	

Table 1- Baseline demographic data

Outcome measures		Test group (n=30)		P value
		BT	AT	
Primary outcome	**ICIQ-UI SF**	13.80±2.30	3.20±2.62	<0.001
Secondary Outcome	**PERFECT-score**			
	Power	2.27±0.78	3.70±0.47	<0.001
	Endurance	4.53±1.07	7.00±0.98	<0.001
	Repetition	4.20±0.85	6.57±0.97	<0.001
	Fast	4.77±0.77	6.83±1.02	<0.001
	Stress test	1.00±0.00	0.00±0.00	<0.0001

Table 2- Data for clinical outcome measures

ICIQ score	BT	AT	1FU	% change
0	0(0%)	10(33.3%)	5(16.7%)	16.7%
1-5	0(0%)	12(40%)	15(50%)	50.0%
6-10	3(10%)	8(26.7%)	10(33.3%)	33.3%
11-15	19(63.3%)	0(0%)	0(0%)	-63.3%
16-21	8(26.7%)	0(0%)	0(0%)	-26.7%
Total	30(100%)	30(100%)	30(100%)	-

Table 3- % change in ICIQ-UI SF score

DISCUSSION

The incidence of SUI is strongly related to increasing age especially but now it also confirmed in only young and middle-aged women. The Mean±SD of age of the participants included in the study were 42.67±8.21. Maximum number of patients belongs to age group of 30-40 (46.7%) (table1). This higher incidence in young and middle aged women may be attributed to the higher level of physical activity seen in younger women than that of older women. 66.7% (n=20) patients were of *balghami mizaj* (cold temperament). This finding confirms the writings of ancient unani scholars that *salas al-bawl* is commonly seen in *balghami mizaj* (phlegmatic temperament).[9,10] The mean BMI in this study is 26.25±2.10 kg/m^2 and maximum number of participants belongs to group of 25-30(66.7%) shows that the greatest number of women in the overweight and obese categories had stress urinary incontinence. Mean±SD of parity was 2.8±1.095, there was no relationship between the number of pregnancies resulting in vaginal deliveries per woman and the incidence of SUI. (table 1)

The data presented in this paper represents the first prospective, ever completed study for *Majun kundur* in the management of SUI. All of the primary and secondary outcome measures were showed significant improvement after completion of trial. In this study ICIQ-UI SF questionnaire is main therapeutic outcome Mean±SD of ICIQ-UI SF questionnaire before and after treatment was 13.80±2.30 and 3.20±2.62 with P-value of <0.001 (table 2). A previous study using *kundur(Boswellia serrata)* and *saad kufi(Cyperus*

scriosus) plus pelvic floor muscle training(PFMT) found similar results with Mean±SD before and after treatment was 10.23±0.96 and 3.03±3.67 respectively(Padamja et al., 2013)[21]. Present study shows highly significant improvement in symptoms and quality of life of patients but, at after treatment follow up (12th week) Mean±SD was slightly increased to 4.03±2.68 with P value 0.001. As at commencement of treatment 90% patient were suffered from severe SUI but after treatment 10(33.3%) patients shows complete cure with ICIQ score-0 and 12(40%) patients having slight incontinence with ICIQ score 1-5 and 8(26.7%) patients improved up to the moderate category with score of 6-10, hence, there was not a single patient with severe incontinence left after treatment and even at after treatment follow up visit. Here at after treatment follow up symptoms recurred slightly because of discontinuation of treatment which shows duration of treatment should be enhanced (table 3). Present study also shows highly significant improvement in all attributes of PERFECT score. Provocative stress test shows 90% improvement as it was positive in 30(100%) patients before treatment, and after treatment it was positive only in 3(10%) patients with P value of <0.0001, considered strongly significant (table 2). At after treatment follow up it exhibits 70% improvement as now stress test was positive in 9(30%) patient. Therefore we can conclude that these data shows significant improvement in SUI as only stress test is sufficient for diagnosis of SUI.

Over all resulting data clearly proved the statement of unani scholars, that *Majun kundur* is efficacious in the management of SUI. this *majun* prepared with *baloot(Quercus incana), zanjabil (Zinjiber officinale), saad kufi (Cyprus rotundus),filfil siyah(Piper nigrum), qust (Saussurea lappa),kundur (boswellia serrata)* and relief in the chief complaint of SUI is due to properties of drugs like *qabidh* (astringent), *mujafif* (desiccant)and *muqawwi asab, qalb, mathana*(brain tonic, cardiac tonic, strengthening of bladder)), *jazib* (desiccant), *muhallil* (anti-inflammatory) etc. exact mechanism is not known but these drugs, because of above mentioned properties, cause strengthening of bladder muscles and pelvic floor muscles and as these drugs act as brain tonic which might probably have acted by activating pudendal motor neurons that increase the urethral striated muscle tone and the force of sphincter contraction[21]. Chemical constituents of these drugs like tannin, catechins and flavonoids provide strength to pelvic floor muscles, which strengthen the pelvic floor muscles and prevents the leakage of urine.[22, 23] No adverse effect of test drug formulation was observed during the trial.

Safety profile was within normal range ascertaining the safety of test formulation.

The results of the study have certain limitations due to small sample size of patients, shorter duration of intervention and also lesser duration of follow-up period.

ACKNOWLEDGEMENT

The study was supported by National institute of unani medicine, Bengaluru.

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