A Clinical study on the management of Mutrakrichchra with Trikantakadya Guggulu

Shailesh V Deshpande [1], Vaishali Deshpande [2], Payjani Dubey *[3], Janhavi patharkar [4].

[1] Professor and Head, Department of Kayachikitsa, Parul Institute of Ayurved, Parul University, Vadodara, Gujarat, India.

[2] Professor and Head, Department of Kayachikitsa, Parul Institute of Ayurved and Research, Parul University, Vadodara, Gujarat

[*3] PG Scholar, Department of Kayachikitsa, Parul Institute of Ayurved, Parul University, Vadodara, Gujarat, India.

[4] Assistant Professor, Department of Kayachikitsa, Parul Institute of Ayurved, Parul University, Vadodara, Gujarat, India.

Corresponding Author: Dr Payjani Dubey, PG Scholar, Department of Kayachikitsa, Parul Institute of Ayurved, Parul University, Vadodara, Gujarat, 7748084342, **E-Mail:** payald613@gmail.com

ABSTRACT

The disease 'Mutrakrichchra' has cardinal feature of burning micturition. Thus, needs recognition to explore the newer therapeutic possibilities. It resembles Urinary Tract Infections in modern parlance which is major health problems affecting millions of each year and frequent visits are seen in OPD in day to day practice. The present study is undertaken to evaluate the efficacy of Trikantakadaya Guggulu in the management of Mutrakrichchra. to Urinary Tract Infections. Objective: To evaluate the therapeutic effect of Trikantakadya Guggulu individually in patients suffering from Mutakrichchra. Study Design: Prospective open labelled clinical study conducted in daily clinical practice Methods. Subjects were advised to take "Trikantakadya Guggulu" 1500 mg TDS for 14 days with Anupana Luke warm water. 30 subjects completed the study. The primary endpoints were changes in urine routine microscopic in pus cells. The secondary outcomes were dysuria, pain reduced. Results- At baseline visit the mean value of pus cell 14.7 ± 6.54 which reduced highly significant 4.93 ± 4.55 on day 14. The mean value of Epithelial cells at baseline 4.967±6.505 which reduced significantly 2.800 ± 3.347 on day 14. The mean score of RBCs at baseline 0.667 ± 0.758 which reduced significantally 0.433 ± 0.568. Vitals and all the safety laboratory parameters were within normal limit both at baseline and day 14th. Conclusion Trikantakadya Guggulu is safe and significantly effective in reducing, pus cells dysuria, pain and burning micturition CTRI registration No is **CTRI/2019/02/017741.**

KEY WORDS: Trikantakadya Guggulu, Mutrakrichchra, clinical study.

INTRODUCTION

The disease 'Mutrakrichchra' is described in all major classical textbooks of Ayurveda. Detail information regarding various aspects of the disease are available in the different textbooks of ayurveda. This infers the existence of Mutrakrichchra since the inception of medicine in India.

The *krichchra, dahayukta* and *muhurmuhur mootra pravritti* are the common clinical conditions in daily practice. These particular observations necessitated to under take this work for dissertation [1].

The disease *Mutrakrichchra* is documented in classical text of Ayurveda. Ayurveda gives guidelines to treat this confidently and increase quality of life of an individual. There are different Modalities for management of *Mutrakrichchra.*

The pittaja variety of Mutrakrichchra assimilates more to Urinary Tract infections in modern parlance on theoretical and clinical symptomatology of the disease. UTI is acute condition and reoccurs in many cases. It is very difficult to treat with single drug. So here multiple drugs are used to treat all types of infectious conditions in LUTI, irrespective of infective organisms [2].

UTI i.e. Bacterial UTI is one of the most common, painful and annoying cause of health, usually by E. coli, affecting any part of urinary tract especially lower tract.

UTI's are one of the leading causes of morbidity and health care expenditures in persons of all ages. Each year UTI's account for 9.6 million doctor visits. Women are especially more prone to UTI. One in five women develops UTI during her life time. Sexually active young women are disproportionately affected. UTI in men are not so common but they can be serious when they occur.

MATERIALS AND METHODS:

This study was approved by Institutional ethics committee (IEC) of Parul institute of Ayurved Parul University ,Vadodara Gujarat on 04/01/2019. The study was conducted between jan 2019 and jan 2020 in accordance with GCP Guidelines.

Informed consent an informed written consent was obtained from all subjects before any study related procedure. The consent form was prepared in accordance with the guidelines oh WHO Research Ethics Review Committee (ERC) Ethical clearance

- Ethical clearance was obtained from institutional ethic committee of Parul Institute of Ayurved ,Parul university Vadodara- 391760 vide Ref- PU/PIA/IECHR/2019/46 Dated on 04/01/19.
- Registration

This study was registered in clinical trial Registry of India (CTRI;www.ctri.nic.in) vide CTRI/2019/02/017741. Date- 20/02/2019.

Inclusion criteria

- People of age group 20-60 years, of either gender, irrespective of caste, religion, socio-economical status.
- Patients diagnosed with mutrakrichchra based on signs symptoms - .
- Positive urine microscopy (pus cells≥10/hpf) in centrifuged mid-stream urine.

Exclusion criteria

- UTI with secondary systemic disease like renal failure,
- Uncontrolled systemic disease - Diabetes Mellitus Hypertension & any anatomical abnormalities.
- Pregnant and lactating women.

Sample size calculation was based on assumption a sample size of 30 evaluable cases provides 80% power to estimate the reduction of mean change in Mutrakrichchra on pus cells. In subjective criteria 5% level of significance.

- Objective criteria
- Changes in Urine routine and microscopic examinations before treatment (at baseline) and after treatment (at 14^{th} day)

Subjective Criteria:

• Symptoms of mutrakrichchra were assessed before and after treatment. For the assessment of these symptoms scoring pattern adopted.

Mutradaaha (Burning Micturition)

▪ No burning micturition	0
▪ Occasional burning micturition	1
▪ Occasional burning micturition, required treatment	2
▪ Constant burning micturition required treatment	3
▪ Constant severe burning micturition but did Not show relief even After treatment	4

Dysuria

▪ No dysuria	0
▪ Occasional dysuria	1
▪ Occasional dysuria which require treatment	2
▪ Constant dysuria which require treatment	3
▪ Constant severe dysuria but did not show relief even after treatment	4

Muhurmutra (Urine Frequency)

▪ 1 to 2 times	0
▪ 3 to 6 times	1
▪ 7 to 9 times	2
▪ 10 to 15 times	3
▪ More than 15 times-	4

❋ Ruja (Pain)

▪ No pain	0
▪ Occasional pain did not require treatment	1
▪ Occasional pain but, required treatment	2
▪ Constant dull ache pain, required treatment	3
Occasional pain did not require treatment	4

Enrolled 33 patients in this study 30 subjects' completers. On screening visit subject written informed consent was obtained, demographic data were recorded. Disha Prakriti, pariksha, general and systemic examination were done. History of any concomitant medical illness was recorded; Subjects underwent investigations urine routine microscopic was assessed. Burning micturition, dysuria, pain, Frequency of Urine recorded in the CRF subjects. On baseline visit and follow op visit subjects underwent general and systemic examination. Subjects were assessed for Burning micturition, Dysuria, frequency of urine. One small box of Trikantakadya Guggulu provided to subject (70 tablet compositions details are provided in table no 1) Ingredients of Trikantakadya guggulu:

Table. 1:

S.NO	SANSKRIT NAME	BOTANICAL NAME	PART USED	PROPORTION
1	Haritaki	*Terminalia chebula*	Fruit	1 part
2	Vibhitaki	*Terninalia bellerica*	Fruit	1 part
3	Amalaki	*Emblica officinalis*	Fruit	1 part
4	Shunthi	*Zingiber officinale*	Fruit	1 part
5	Marich	*Piper nigrum*	Fruit	1 part
6	Pippali	*Piper longum*	Fruit	1 part
7	Nagarmotha	*Cyperus scariosus*	Tubers	1 part
8	Gokshur	*Tribulus terrestris*	Fruit	1 part
9	Gugglu	*Commiphora mukul*	Resins	1 part

CRF subjects were closely monitored for any adverse event. Tolerability of the study drug was assessed by the investigator and subjects at the end of study. Investigations were repeated at the end of study.

OBSERVATIONS

Observations	No of patients	Total
Age (Mean ± SD)	40.303 ± 12.665	-
Gender Male/female	15/18	33
Religion Hindu/muslim	30/3	33

Bowel habit Regular/irregular	24/9	33
Kostha Mrudu/madhyam/krura	6/20/7	33
Diet Mixed/veg	25/8	Total
Prakruti Vata-Pitta/Kapha-Vata/Kapha-Pitta/Pitta -kaphaja	14/4/2/11	-
Menstrual history Regular/irregular/menopause	11/2/4	33
Vyayama Regular/irregular	21/12	33

Summary statistics were used to analyze the subjective criteria such as Burning micturition, dysuria, frequency of urine, pain were assessed by Wilcoxon's, Friedman's test. The efficacy and safety parameters were analyzed by using student t-test. All p values were reported based on two sided significance test and all the statistical tests were interpreted at 5% level of significance. Significant changes in pus cells, epithelial cells, RBCs from day 7 to day 14. The result observed on Burning micturition, frequency of urine, dysuria, and pain except frequency of urine significant changes in burning micturion, dysuria and in pain. No any patients required any reuse medicine for Mutrakrichchra.

Adverse event such as fever recorded in only 1 subject during post treatment treated with proper medication for fever [3].

Table 2:

Parameter	Before treatment (at baseline) Mean ±sd	After treatment Mean ±sd
Pus cells	14.7 ± 6.54	4.93 ± 4.55 P value (<0.001)
Epithelial cells	4.967 ± 6.505	0.433 ± 0.568

		P value (<0.050)
RBCs	0.667 ± 0.758	0.433 ± 0.568 P value (<0.050)

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Effect of therapy on subjective and objective parameters,

Effect of Therapy in burning Micturition

Effect of Therapy in burning Micturition: Mean score for burning micturition prior to the treatment was 3.700 which reduced to 2.733 after the treatment with mean difference 0.967. The change that occurred with the treatment is greater than would be expected by chance, this improvement when analysed by paired 't' test found to be significant was reduced by 26.13% which was statistically significant (<0.001).

Parameter	Mean Rank	N	DF	X^2	Pvalue	S.D
Burning_micturition BT	2.92	30	2	53.226	0.0000	0.79438 0.82768
Burning_micturition_follow_up	1.93					
Burning_micturition_AT	1.15					0.8874

Parameter		N	P value
Burning_micturation_follow_up - Burning_micturation_Bt	Negative Ranks	27[a]	.000
	Positive Ranks	0[b]	
	Ties	3[c]	
	Total	30	
Burning_micturation_At -	Negative Ranks	22[d]	.0000
	Positive Ranks	0[e]	

Burning_micturation_follow_up	Ties	8[f]	
	Total	30	
Burning_micturation_At - Burning_micturation_Bt	Negative Ranks	30[g]	.0000
	Positive Ranks	0[h]	
	Ties	0[i]	

Effect of Therapy in Dysuria: Mean score for dysuria prior to the treatment was 3.467 which reduced to 1.567 after the treatment with mean difference 1.900. The change that occurred with the treatment is greater than would be expected by chance, this improvement when analysed by paired 't' test found to be significant was reduced by 54.80% which was statistically significant (<0.001).

Descriptive Statistics

	Mean rank	N	X^2	DF	S.D	P Value
Dysurea_Bt	3.4667	30	.93710	2.	0.93710	0.000
DysureaFolow_up	2.533		.93710		0.93710	
Dysurea_At	1.5667				0.89763	

Parameters		N	P
Dysuria_follow_up - Dysuria_BT	Negative Ranks	26[a]	
	Positive Ranks	0[b]	0 .0000
	Ties	4[c]	
	Total	30	
Dysuria_at - Dysuria_follow_up	Negative Ranks	23[d]	0. 0000
	Positive Ranks	0[e]	
	Ties	7[f]	
	Total	30	
Dysuria_at - Dysuria_BT	Negative Ranks	28[g]	
	Positive Ranks	0[h]	0.0000

RESULTS

A total of 33 patients were screened for recruitment, out of which 30 were found eligible and recruited in the study.30 subjects completed study out of which 15 were male (45.45%) and 18 were female (60%) .The mean age was 40.303 ± 12.665 . The mean pus cells reduced significantally 14.7 at baseline after treatment it was 4.93. The mean epithelial cells reduced significantally 4.97 at baseline after treatment it was 2.800. The mean RBCs (red blood cells) reduced significantally0.667 at baseline after treatment it was 0.433. Significant changes in burning micturition, dysuria, and pain.Non significant result in frequency of urine. No significant changes from baseline to end of therapy in values of any vital signs (pulse rate, respiratory system, body temperature, systolioc and diastolic blood pressure

DISCUSSION

Sadaha mootrapravruti (burning micturition): Sadaha mootrapravruti (burning micturition) On first day all 30 patients had Sadaha mootra pravrutti and it was the main complaints of those patients .so it is considered as main symptom of UTI. 30 patients had severe burning micturition grade 4. on 7th day 3 patients had severe burning micturition 19 patients had mild burning micturition, 7 patients had occasional burning micturition, after 14th No any patient had severe burning micturition grade 4, 19 patients had occasional burning micturition burning micturition 8 patients had mild burning micturition.

After one month of treatment there were 13 patients were completely free from Sadaha mootrapravritti. The result is statistically highly significant. Daha is the main symptom of pitta prakopa. It is found that majority of ingredients are having Madhura vipaka and Sheeta veerya act as pittashamaka [4].

Discussion on Sashool Mootrapravruti (pain): On first day all 30 patients had sashool mootra pravrutti and it was the chief complaints of those patients .so it is considered as symptom of UTI. 6 patients had severe pain,9 patients had mild sashool mootra pravrutti, 2 patients had occasional sashool mootra pravrutti. On 7th day no patients had severe sashool mootra pravrutti 6 patients had mild sashool mootra pravrutti, 11 patients had occasional sashool mootra pravrutti,14 patients had no sashool mootra pravrutti after 14th No any patient had severe & mild sashool mootra pravrutti,14 patients had occassional pain, 16 patients were free from pain. The p value is 0.001 which is statistically highly significant. Some ingredients in the present study were having Vedana Stapaka properties such as Shunthi, Pippali, Maricha, etc. Decrease in Sashoola Mootrapravritti is appreciable from these medicines.

Discussion on kruchchmootrata (dysuria): On 1st day total 19 patients had grade 4 severe pain Kruchchmootrata 9 patients had mild Kruchchmootrata, 2 patients had occasional Kruchchmootrata on 7th day 2 patients had grade 4 kruchchmootrata, 17 patients had mild kruchchmootrata,11 patients had occasional kruchchmootrata, after 14th day no any patients had grade 4 Kruchchmootrata, 5 patients had mild Kruchchmootrata, 3 patients had no pain, 22 patients had occasional Kruchchmootrata.

Discussion on Muhur Mootrata (frequency of urine): Frequency of micturition was severe in 0 patients, moderate in 1 patient, mild in 21 patients, and normal in 8patient on 1st day. On 7th day no any patients was in grade 4 moderate in 1 patients, mild in 16 patients and normal in 13 patients, On 14th day no any patients were in grade 4, moderate in 1 patient, mild in 16 patients and normal in 13 patients.

INVESTIGATIONS

Microscopy of urine was done before the treatment and after completion of the treatment. All the patients had

plenty of pus cells in urine before treatment. After 14 days of treatment 15 patients were cured completely and 15 patients pus cells reduced but not totally cured. The result were highly significant with P value 0.000.

Probable mode of action: In Ayurvedic formulations the drugs act combined, while pacifying one dosha it does not vitiate other. Some herbs enhance the action while others avoid or minimize possible side effects.

Plants are complex mixtures of various compounds; one ingredient may be principally responsible for an action, and where as other secondary components may be just as important activators or modifiers of this action. The interaction of a variety of compounds makes remedies more effective. Thus the formulations *Trikantakdaya guggulu* were selected, which comprises multiple constituents help the formulations to function as a whole.

Effect of Haritaki and vibhitaki on Mootradaaha (Burning micturition): It showed antibacterial and anti fungal activity [1], inhibits the growth of E. coli, the most common organism responsible for UTI. It also showed antibacterial activity in Urinary tract infection. Haritaki due to its Madhura and tikta rasa acts as a Pittaghana and due to Madhura Rasa and Ushna Veerya it does vata shaman and Tridoshahar property. Vibhitaki due to its Madhur Vipaka, Kasahaya rasa and Laghu guna, ushna Virya it acts as a Rasayana, Krimighna property.

Effect of Amalaki on Mootradaaha (Burning micturition): *Amalaki* due to *its Madhura Vipaka* , and *Sheet Virya* it acts as *Pittaghana* reduced *Mootradaaha* (burning micrurition) .Bhattacharya et al *Triphala* have reported varying degrees of strain specific anti-bacterial activity against multidrug resistant uropathogenic bacteria.

Effect of Shunthi on Rooja (pain): Shunthi due to its Katu Vipaka, Ushna Virya it normalizes Apana Vata , reduced *Tivra Rooja* (pain) in Vankshan Its chemical constituents like 10- Gingerdione, 6- Gingerdione, Gingerenone- B, Gingerenone-c it acts as a antibacterial activity against s.aureus, e.coli.

Effect of pippali on Kruchmootrata (Dysuria): Pippali, Marich is having Laghu and snigdha, Guna, Katu rasa Ushna Virya it Removes Sanga due to all this property it relieves Mutrakrichchra. Its chemical composition is piperine it acts as a antimicrobial activity, antibacterial activity against e.coli, s.aureus.

Effect of Guggulu in Kruchchmootrata (dysuria): Guggulu acts as *Deepana, Amapachana, Strotosodhana* due to its Katu Vipaka, Katu Rasa and Ushna Virya. Sanga is removed in Mutravaha strotas particularly in Basti Sira, its free from *Avarodha*, the Apana Vayu normalizes and its relieves *Kruchchmootra [1].* Its active compound are alkaloids, steroids, terpenoids it acts as antibacterial it cures urinary tract infection.

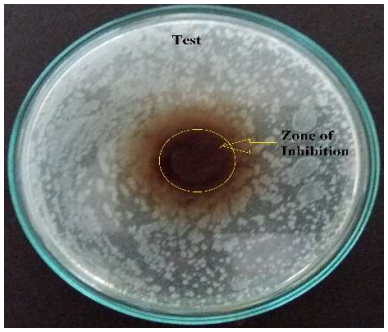
Effect of Gokshur in Mootradaaha (burning micturition): *Gokshur* is having *Madhura Rasa* and *Snigdha Guna which is* Kaphakara which leads to increase in kleda. leading to mutra Kapha is responsible for increase in kleda leading to *Kruchchmootrata*(dysuria) reduced. It is also mentioned in *Daahprashaman Mahakashaya* because of this property it reduced *Pitta* in *Basti* Pradesh and also reduced *Mootradaaha* (burning micturition). *Tribulus terresteris* active compounds is saponin it acts as a antibacterial activity [3], antiviral due to all this properties it cures urinary tract infection.

Musta Mootradaaha (burning micturition): *Musta* is having *Laghu Guna*, *Katu Vipaka*, *Sheet Virya* it act as *Deepana, Pachana* , it removes *Sanga* of Mootravaha Strotas. It is mentioned as *Mootrasangrhniyanaam*, due to all these properties it releives *Mutrakrichchra Cyperus rotundus* active compound is butanol it acts as a antibacterial activity against E. coli.

Methodology- In vitro study: Prepare nutrient agar plate Inoculated with E.coli, with a depth of 4-5 mm and then it allow it to solidify. Then with the help of sterile borer make cavity in centre of plate Then in test plate fill that cavity with Formulated tablet (*Trikantakadya guggulu*) in Crushed Form. In case control plate fill that

cavity with standard antibiotic solution. Then slowly incubate the plate at 37*c for 24 hrs. After incubation measure the Zone of inhibition.
Zone of inhibition.test plate show average 0.3 cm Zone of inhibition. *Trikantakadya Guggulu* shows antimicrobial effect against E.Coli.

RESULT



Control Plate (Amoxicillin 0.3µg/ml) Test plate with formulation

DISCUSSION

The *Trikantakadya Guggulu* (powder form) produced 0.3 cm zone of inhibition against E.coli.It was found that the *trikatu* extract (*shunthi,marich,pippali*) antibacterial activity was classified as >20 mm zone of inhibition against e.coli, *Triphala* (*haritaki,vibhitaki,amalaki*) antibacterial activity was classified as moderate zone of inhibition against e.coli, *guggulu* (*commiphora mukul*) extract antibacterial activity shows 12 mm zone of inhibition.

Significant changes in pus cells, epithelial cells , RBCs fron day 7 to day 14 .The result observed on Burning micturition, frequency of urine, dysuria,and pain except frequency of urine significant changes in burning micturion, dysuria and in pain.No any patients required any resue medicine for Mutrakrichchra [6].

Adverse event such as fever recorded in only 1 subject during post treatment treated with proper medication for fever.

CONCLUSION

Mutrakrichchra is *Pakwashaya samutha* shoola yukta *Daha Pradhan* Madhyama Rogamarga Samanyaja vyadhi. The role of *Krimi* as a causative factor of *Pittaja Mootrakruchra* is not been mentioned in classics. *Pittaja Mootrakruchra* can be compared to lower urinary tract infection.

In over all study the patients observed with *Peeta mootrata, Saruja*, *Sadaha, Kruchra*,*Muhur Muhur Mootra Pravrutti* and few of *Sarakta* Mootrapravrutti.and maximum number of results found in vataja mutrakrichchra.

While explaining the Vishamajwara bhootanubandha is explained and it is considered as *Savisha Krimi* by Chakrapani which is invisible due to *Atisoukshmyat.* This can be incorporated for infection in context of Mutrakrichchra also. Chance of recurrence and drug resistant cases are more common in LUTI.

Single drug therapy is not sufficient. Multiple drugs which are having multiple actions like diuretics, antimicrobial, immuno-modulating action are used in present study.

So this formulation have given good effect with statistically highly significant results. The P value is of 0.000.

Ethics Approval and Consent to Participate: Not applicable.

Human and Animal Rights: Necessary Permissions obtained from the regulatory authorities.

Conflict of Interest: The authors declare no conflict of interest.

Acknowledgment: None

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