Innovare Academic Sciences

International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 7, Issue 2, 2015

Original Article

EFFECT OF MENTHA PIPERATA IN EXPERIMENTAL PROSTATIC HYPERPLASIA IN WISTAR ALBINO RATS

Y ROJA RAMANI, BENU PANIGRAHY[1], SWAPNA ROHIT SAHU, SAILEN KUMAR MISHRA

Assistant Professor, Department Of Pharmacology, [1]Department of Urology, MKCG Medical College, Berhampur University, Berhampur. Email: yrramani@yahoo.com

Received: 30 Oct 2014 Revised and Accepted: 22 Nov 2014

ABSTRACT

Objective: To investigate the protective efficacy of *Mentha piperata* in experimental benign prostatic hyperplasia in Wistar albino rats.

Methods: Benign hyperplasia of prostate was induced by subcutaneous injection of testosterone (5mg/kg) daily for 28 days. Rats were divided into five groups (six rats each). A negative control group received subcutaneous arachis oil (1 ml/kg), Four groups were injected testosterone and divided into reference group (finasteride 1mg/kg), modelgroup(testosterone), study group A (*M. piperata*200mg/kg) and study group B (*M. piperata* 400mg/kg). On day 29, rats were sacrificed and body weight, prostate weight, bladder weight, testes weight, serum testosterone and total protein in prostate were measured and histopathological studies carried out. All results were expressed as mean ± SEM. Data were analysed by one-way analysis of variance followed by Tukey'spost hoc test.

Results: *M. piperata*(400mg/kg) significantly inhibited prostate growth and total protein content($P < 0.05$). The extract did not have significant effect on serum testosterone level, weight of testes and bladder. Histopathological analysis of prostate gland correlated with the above results.

Conclusion: Beneficial effects of *M piperata* in various common ailments have been proven through various studies. The findings of this study suggest a possible beneficial effect of *Menthapiperata* in the prevention of benign hyperplasia of prostate.

Keywords: Benign prostatic hyperplasia, Dihydrotestosterone, *Menthapiperata*, Prostate gland, Testosterone.

INTRODUCTION

Benign prostatic hyperplasiais a non-malignant, uncontrolled proliferation of epithelial cells and stroma that occurs in the peri-urethral transition zone of prostate gland that surrounds the urethra [1]. The exact etiology remains a mystery even as its prevalence continues to grow amongst aged men [2, 3]. Dihydrotestosterone (DHT), an active metabolite of testosterone formed by enzymatic conversion mediated by 5α reductase is believed to promote prostate growth. Elevated estrogen levels and augmented adrenergic tone [4] in prostate smooth muscle are also believed to play a role in the development disease.

The road to cure is a long and tiresome one and includes watchful waiting, drug treatment and surgery. Available classes of drugs include 5α reductase inhibitors and α adrenergic antagonist but they are not without side-effects ranging from impotence and gynaecomastia to orthostatic hypotension and abnormal ejaculation [5]. Surgery though a sure method is costly and elderly may not be compliant.

India is home to an array of medicinal herbs that includes several with anti-fertility and anti- androgenic effects like *gossypol, ocimum, papaya*to name a few. *Menthapiperata* (peppermint), an age old remedy for indigestion, common cold, bronchitis, sinusitis etc, has of late gained importance for its anti-androgenic and antifertility activity [6,7].

With this background information the present study was carried out to explore effectiveness of *Menthapiperata* in experimental BPH in rats.

MATERIALS AND METHODS

Animals

30 Male Wistar albino rats (120-180g b. w) were used. They were housed in polypropylene cages, maintained in room temperature (25±1°C), humidity of 45-55% under 12-hlight & dark cycle. Animals were allowed a week's time to acclimatize with the laboratory conditions before the study with free access to food and water ad libitum. All experimental procedures were carried out in accordance with Committee for the Purpose of Control and Supervision of Experiments in Animals (CPCSEA) guidelines. The study was reviewed and approved by Institutional Animal Ethical Committee. Animals were randomly divided in different groups for different treatments.

Plant extract and drugs

Menthapiperata, Finasteride, and testosterone were obtained as gift samples from SSS Biotic Pvt. Ltd. Bhubaneswar, Dr Reddy's Laboratory and Infar Pharmaceuticals respectively.

Experimental design

In the table.

Induction of disease

Male Wistar rats weighing 120-180g were randomly divided in five groups (n=6). Experimentally developed BPH model was created by subcutaneous injection of testosterone (5mg/kg) dissolved in arachis oil for 28 days.

Menthapiperata was dissolved in distilled water and orally administered once daily for 28 days. Weekly measurement of body weights was done. On the 29th day, blood was collected from retro orbital plexus under light ether anesthesia following which animals were sacrificed by cervical decapitation. Immediately prostate gland, bladder and both testes were dissected and weighed and various parameters like prostatic index, serum testosterone and total protein were measured.

Prostate weight (P) to body weight (BW) ratio

Prostate weight (P) to body weight (BW) ratio was calculated by dividing prostate weight with that of animal body weight for the individual study group animal.

Determination of serum testosterone level

Blood samples were collected and centrifuged at 2000rpm for 20 mins to obtain serum for testosterone using enzyme-linked immune-sorbent assay kit (C. L. I. A)

Determination of total protein in prostate

Prostate glands were dissected and homogenates were made in phosphate buffer solution (0.01M sodium phosphate buffer, pH 7.4, containing 0.14 M NaCl) at a ml volume/g gland wet ratio of 4:1. Homogenates were centrifuged at 3000rpm for 20 mins and supernatant collected. Supernatant was used as a source of proteins and concentration was determined by modified biuret end point assay method.

Histopathological investigation

All prostatic specimens in each group were fixed with 10% formalin and histopathological investigation was done.

Percentage of recovery

On the basis of mean prostatic weight and P/BW ratios, percentage recovery in P/BW ratio by test group compared with model group was calculated. The increase induced by testosterone alone was taken as 100% and all other test groups were compared with this reading. Percent recovery by test sample = A-B, where A is the percentage increase in prostatic weight induced by testosterone and B is the percentage increase in prostatic weight induced by test sample.

Statistical analysis

All results were expressed as mean ± SEM. Data were analysed by one-way analysis of variance followed by Dunnett's post hoc test.

Table 1: Shows the different treatment groups in the present study

Groups	Type	Treatment
I	Negative control	Arachis oil 1 mg/kg/day s. c
II	Disease Model	Testosterone 5mg/kg /day s. c in arachis oil
III	Standard group	Testosterone 5mg/kg /day s. c in arachis oil + finasteride 1 mg/kg/day p. o
IV	Extract treated group 1	Testosterone 5mg/kg /day s. c in arachis oil + *M. piperata 200 mg/kg*/day p. o
V	Extract treated group 2	Testosterone 5mg/kg /day s. c in arachis oil + *M. piperata 400 mg/kg*/day p. o

RESULTS

Evaluation of prostatic enlargement

Effect of *M. piperata*on prostatic parameters

When animals were treated with testosterone injection (5mg/kg) it showed significant increase in prostate weight and prostatic index compared to negative control group. There was significant change (P<0.05) in prostate weight after treatment with *M. piperata* extract 400mg/kg when compared with model group. [Fig. 2, Table 2]

Effect of *M. piperata*on other parameters

There was no significant difference between bladder weights. But protein levels in prostate gland were significantly altered in extract treated groups compared to model group. Serum testosterone level was significantly increased in model group compared to negative control. Administrations of M. piperata did not significantly affect serum testosterone level. [Table 3]

Histopathological investigation

Histopathology of negative control group showed normal histological features of prostate gland, with aciniand tubules of variable diameter, irregular lumen with single layer of epithelium. The lumen was filled with prostatic secretions in connective tissue, the matrix was normal.

Stroma and gland revealed histology suggestive of normal prostate gland. The group treated with testosterone alone showed mild to moderate disruption of histo-architecture of the gland viz tubules appeared wider with thickened walls, large involutions and narrowed lumen.

Finasteride treated group exhibited features of normal prostate. M. piperata (200 mg/kg) showed loci of disrupted architecture interspersed with areas of normal prostate. But M. piperata (400 mg/kg) showed improvement in histo-architecture compared to model group. [Fig. 3]

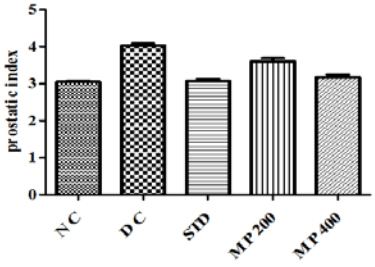

Fig. 1: Effect of menthe piperata on prostatic tndex
NC: normal control; DC: disease control; STD: Standard; MP 200: *Mentha piperata* 200 mg/kg; MP 400: *Mentha piperata* 400 mg/kg

Table 2: Effect of *Menthapiperata on* prostatic parameters

Groups	Animal weight (g)		PW(g)	PW Index (g/g x 1000)	% increase in PW	% Recovery
	Initial	Final				
Group I	146.67 ± 6.79	149.67 ± 6.11	0.46 ± 0.02	3.05 ± 0.03	-	-
Group II	137.50 ± 7.39	139.17 ± 6.50	0.57 ± 0.03	4.03 ± 0.04*	100	-
Group III	137.00 ± 7.11	136.17 ± 5.53	0.43 ± 0.03	3.07 ±0.04**	74.78	25.22
Group IV	145.33 ± 8.70	150.83 ± 8.49	0.54 ± 0.04	3.60 ± 0.08	95.6	4.40
Group V	140.67 ± 7.02	142.50 ± 7.04	0.46 ± 0.02	3.17 ± 0.07**	80.35	19.65

* p< 0.01 compared to negative control, ** p< 0.01 compared to disease model

Table 3: Effect of *Menthapiperata* on various parameters

Groups	Bladder Weight(g)	Testes weight (g)	Serum testosterone (ng/ml)	Total protein (g/dl)
Group I	0.11 ± 0.02	0.66 ± 0.09	3.76 ± 0.05	2.05 ± 0.28
Group II	0.10 ± 0.02	0.41 ± 0.05*	18.75 ± 0.15*	2.88 ± 0.26*
Group III	0.09 ± 0.01	0.61 ± 0.19	15.45 ± 0.2	1.85 ± 0.16**
Group IV	0.09 ± 0.02	0.53 ± 0.14	17.05 ± 0.04	2.70 ± 0.20
Group V	0.10 ± 0.02	0.53 ± 0.12	16.9 ± 0.3	1.93 ± 0.14**

* p< 0.01 compared to negative control, ** p< 0.01 compared to disease model

Fig. 2: Hypertrophied prostate of albino rat

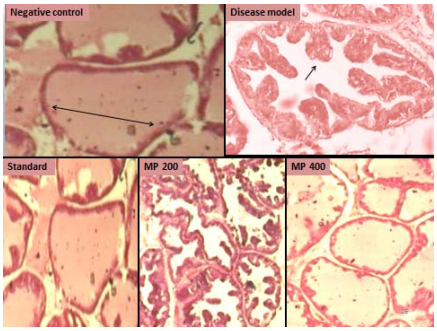

Fig. 3: Histopathology of prostatic tissue in different groups

DISCUSSION

Benign prostatic hyperplasia is one of the geriatric urological disorders where extensive research is going on both in experimental animals as well as through drug trials. Several novel treatment modalities exist for this disease. Recently the focus has been shifted towards herbal remedies for the added benefit of having less adverse effects as compared to the conventional therapy. Herbal medicines like *Menthapiperata* are increasingly used among general population in developing countries.

Induction of prostatic hyperplasia in experimental animals is done by administering testosterone [8, 9]. Male gonadal hormones have a definitive role in this condition. In the present study s. cinjection of testosterone to wistar albino rats significantly increased the prostatic index, total protein content, showed hyperplasia of glandular tissue as well as stroma, and reduced the testicular weight with no significant effect on the bladder weight. The increase in testicular weight may be attributed to the feedback inhibition of hypothalamo-pitutiary axis as a result of increased free testosterone. Finasteride (1mg/kg/day) p. o, significantly decreased the prostatic index and total protein content compared to the testosterone alone group. The histopathological architecture showed less hyperplasia of glandular tissue with no significant effect on the testicular weight and bladder weight.

Menthapiperata was administered in two different doses of 200 and 400mg/kg p. o. The lower dose of *Menthapiperata* did not show significant effect on any of the prostatic and other parameters (table -2 & 3). But at a dose of 400mg/kg p. o it significantly reduced the prostatic index and total prostate protein compared to the disease model. The reduction in total protein content could be explained because of enzymatic changes in the prostate gland. The serum testosterone, bladder and testes weight showed no significant change compared to the testosterone alone. The effects of the higher dose of *Menthapiperata* were comparable to that of Finasteride. Also the findings of the present study are in agreement with other herbal remedies used for the treatment of BPH [10].

CONCLUSION

Beneficial effects of *M piperata* in various common ailments have been proven through various studies. Recent literatures have explored the antifertility and anti-androgenic activity of this herb. The findings of this study suggest a possible beneficial effect of *Menthapiperata* in the prevention of benign hyperplasia of prostate. Further in-vitro and phyto-analytical studies are warranted for isolation of active ingredients and to substantiate our results.

CONFLICT OF INTERESTS

Declared None

REFERENCES

1. Dhingra N, Bhagwat D. Benign hyperplasia: an overview of existing treatment. Indian J Pharmacol 2011;43:6-12.
2. Kirby R. Improving lower urinary tract symptoms in BPH. Practitioner 2011;255:15-9.
3. Stroup SP, Palazzi-Churas K, Kopp RP, Parsons JK. Trends in adverse events of benign prostatic hyperplasia (BPH). B J U Int 2012;109:84-7.
4. Muramatsu I, Oshita M, Ohmura T, Kigoshi S, Akino H, Gobara M *et al*. Pharmacological characterization of of alpha 1-adrenoceptor subtypes in the human prostate: functional and binding studies. Br J Urol 1994;74:572-8.
5. Oelke M, Kuczyk MA, Herrmann TR. Medikamentose therapie der benignen prostatahyperplasie. Urologe 2009;48:1365-77.
6. Gupta RS, S Rakhi. A Review of medicinal plants exhibiting antifertility activity in males. Nat Prod Radiance 2006;5(5):389-410.
7. M Akdogan, M Ozguner, A Kocak. Effects of peppermint teas on plasma testosterone, follicle-stimulating hormone and luteinizing hormone levels and testicular tissue in rats. Urol 2004;64(2):394-8.
8. Veeresh Babu SV, Veeresh B, Patil AA, Warkr YB. Lauric acid and myristic acid prevent testosterone induced prostatic hyperplasia in rats. Eur J Pharmacol 2010;626:262-5.
9. Sun H, Li T J, Sun LN, Qiu Y. Inhibitory effect of traditional Chinese medicine ZiShen Pill on benign prostatic hyperplasia in rats. J Ethnopharmacol 2008;115:203-8.
10. Shrivastava A, Gupta VB. Various treatment options for benign prostatic hyperplasia: a current update. J Mid-Life Health 2012;3(1):10-9.