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COLLABORATIVE RESEARCH

Evidence based clinical study to assess the usefulness of homoeopathic medicines in patients of Benign Prostatic Hyperplasia

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Background and Objectives: Benign Prostatic Hyperplasia (BPH) is the most common condition in elderly men and its incidence is age related. Although clinical evidence of disease occurs less commonly, symptoms of prostatic obstruction are also age related and if untreated affect quality of life. No data regarding clinical as well as diagnostic parameters assessment in the cases of BPH in response to homoeopathic medicines is available. Therefore, an observational study on BPH was conducted with 20 predecided medicines for the treatment of BPH.

Methods: A collaborative research study between Central Council for Research in Homoeopathy (CCRH), New Delhi and Homoeopathic Research Foundation, Lucknow was planned. A total of 121 patients enrolled, out of which 43 completed the study according to protocol. Trial medicines selected on the basis of principles of Homoeopathy were prescribed and International Prostate Symptom Score (IPSS), Ultrasonography, Uroflowmetry and Prostate Specific Antigen (PSA) were assessed before and after homoeopathic treatment.

Results: After comparing pre and post treatment results, the difference in mean values of IPSS, Prostate weight, PSA and Average flow rates were found statistically significant. Maximum Flow Rate and Post Void Residual Urine (PVRU) were found improving but statistically not significant. *Lycopodium* (n=15), *Pulsatilla* (n=11), *Sulphur* (n=8) and *Calcarea carb.* (n=3) were found to be most useful among 10 medicines prescribed.

Conclusion: Results obtained from the study are encouraging with findings that 93.0% of patients improved clinically with an evidence of positive changes in diagnostic parameters. However, such study with randomized control trial is needed to further validate the usefulness of the homoeopathic medicines.

Keywords: homoeopathy; observational study; benign prostatic hyperplasia; international prostate symptom score; lycopodium; pulsatilla; sulphur

Introduction

Clinically BPH is defined as a combination of benign prostatic enlargement with lower urinary tract symptoms and bladder outlet obstruction. BPH symptoms range from least voiding difficulties to urinary retention and renal failure. An estimated 75% of men >50 years of age have symptoms arising from BPH and 20–30% of men reaching 80 years of age require surgical intervention for the management of BPH.[1, 2] Effect due to BPH on quality of life has been found similar to that of other chronic diseases such as diabetes mellitus, hypertension and heart disease.[3, 4] Even depression of mood is more likely to occur in men with BPH.[5] BPH is associated with least mortality, however, the morbidity associated with progression of the disease can be crippling. Preventing the sequelae of BPH is one of the main goals of treatment. Progression of BPH can be assessed by using subjective measures such as changes in IPSS/AUA symptom index or objective measures such as changes in prostate size and urinary flow rate. The successful management and treatment of BPH should seek both to improve symptoms and prevent disease progression.

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Homoeopathy, an outcome of experimental research is based on principle of similia which implies that a drug cures in the sick what it causes in the healthy. As per WHO report, Homoeopathy is 2nd most used health care system in the world.[6] Gupta et al,[7,8] for the first time published their clinical work on BPH in the year 1994 and shown the usefulness of homoeopathic medicines in cases of BPH. Ultrasonographic evaluation of prostate weight was the only parameter for assessment of treatment. No data on role of homoeopathic medicines in patients of BPH in terms of clinical and diagnostic assessment is available. So the present study of BPH was undertaken by Homoeopathic Research Foundation in collaboration with CCRH with 20 pre-selected homoeopathic medicines prescribed on holistic basis to arrive at a group of effective homoeopathic medicines for treatment of BPH.

Objectives

Primary objective

To carry out an open clinical trial for evaluating the usefulness of pre-selected homoeopathic medicines; the selection of which is done on the diagnostic symptoms of 'Benign Prostatic Hyperplasia' and the prescription thereof is based on the characteristic mental/emotional attributes of the patient.

Secondary objectives

1. To determine and verify characteristic symptoms of medicines used.
2. To check the progression of disease.

Material and Methods

Study design

The study was prospective and observational, conducted at Gaurang Clinic and Centre for Homoeopathic Research, Lucknow under the aegis of Homoeopathic Research Foundation funded by Central Council for Research in Homoeopathy (CCRH), New Delhi during the period of July 2006 to September 2009. International Prostate Symptom Score (IPSS), the parameter to assess the intensity of suffering was calculated every two weeks. The IPSS / American Urological Association (AUA) symptom index [10] is detailed in Table 1.

Table 1: International Prostate Symptom Score (IPSS)/American Urological Association (AUA) symptom index

IPSS/AUA Assessment						
Questions	(Circle one Number in each row)					
	Not at all	Less than 1 time in 5 (Rarely)	Less than half the time	About half the time	More than half the time	Almost Always
Incomplete emptying: Over the last month, how often have you had a sensation of not empty your bladder completely after you finish urinating?	0	1	2	3	4	5
Frequency: Over the last month, how often have you had to urinate again less than 2 h after you finished urinating?	0	1	2	3	4	5
Intermittency: Over the last month, how often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5

Contd. ...

Contd.

IPSS/AUA Assessment						
Questions	(Circle one Number in each row)					
	Not at all	Less than 1 time in 5 (Rarely)	Less than half the time	About half the time	More than half the time	Almost Always
Urgency: Over the last month, how often have you found it difficult to postpone urination?	0	1	2	3	4	5
Weak stream: Over the last month, how often have you had a weak urinary stream?	0	1	2	3	4	5
Straining: Over the last month, how often have you had to push or strain to begin urination?	0	1	2	3	4	5
Nocturia: Over the last month, how often did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning?	0	1	2	3	4	5
Sum of 7 circled numbers (AUA/IPSS Symptom score): _____ (Maximum: 35) (1-7 = Mildly Symptomatic, 8-19 = Moderately Symptomatic, 20-35 = Severely Symptomatic)						

To assess the status of progression of disease, per abdominal ultrasonography (for prostate weight and post void residual urine volume), uroflowmetry (for maximum flow rate and average flow rate), digital rectal examination (DRE) and prostate specific antigen (PSA) were done at baseline, after completion of three months and one year. The ethical clearance was obtained from Ethical Committee of CCRH before undertaking the study. The study protocol was prepared in accordance with the Helsinki declaration on human experimentation.

Study participants

Two hundred forty one (241) patients were screened in two years, out of which one hundred twenty one (121), above 50 years of age with signs and symptoms of BPH, PSA level equal to or below 4 ng/ml, presence of smooth firm elastic enlargement of prostate on DRE and a swollen or enlarged prostate weighing more than 20 grams on ultrasonography were found eligible to participate in the study. Out of 120 patients who could not participate, 34 were excluded due to diabetes mellitus, 31 due to various other systemic illnesses [hypertension (25), rheumatoid arthritis (4) and hypothyroidism (2)] , 18 due to less prostatic weight, 9 due to recurrent urinary tract infection, 4 due to prostatic carcinoma, 9 due to raised PSA, 2 due to urethral stricture, 6 because of under treatment for other illness during the last two weeks, and 7 were not willing to give consent. Out of 121 cases enrolled under the study, 44 patients were dropped out by the Project Monitoring Officers due to non adherence to protocol, 23 did not turn up after baseline assessment/investigations, 11 were lost to follow up and finally 43 patients could complete one year duration of treatment at the end of the study. To exclude renal insufficiency, serum urea, serum creatinine, urine routine and microscopic tests were performed at baseline. Patients having acute retention of urine and any other condition leading to emergency were also excluded. The patients were enrolled in the study only after getting their written informed consent.

Selection of medicines

The selection of trial medicines was done by repertorising the symptoms of BPH as mentioned in Harrison's Principles of Internal Medicine (15th edition).[11] The repertorisation was done using the Complete Repertory by Roger Van Zandvoort as the reference book. Considering the fact that the study pertains to the BPH, the drugs given in the first grade (3 points) followed by those in the second grade (2 points) mentioned against the rubrics 'Prostate, swelling' and 'Prostate, enlargement' in the Complete Repertory were short-listed. To further minimize the variables, the specific prescribing symptoms of these medicines have also been worked out after repertorisation of all the relevant rubrics. The twenty trial medicines were *Pulsatilla, Calcarea carb., Staphysagria, Sulphur, Silicea, Medorrhinum, Nitric. acid, Phosphorus, Conium mac. , Baryta carb., Thuja, Argentum nit., Lycopodium, Merc. sol., Hyoscyamus, Pareira brava, Digitalis, Chimaphilla, Apis mel. and Selenium.* These medicines were procured from reputed manufacturing firm. The prescriptions were made out of these 20 medicines guided by totality of presenting signs and symptoms on the basis of 'principle of similia,' using complete repertory with the help of Hompath Classic software12. However, if choice of medicine was other than trial medicines then the patient was not enrolled and sent to general OPD for treatment.

Plan of treatment

Plan of treatment was based on the severity of the discomfort determined by IPSS /AUA symptom index.

Mild to moderate intensity (IPSS/AUA symptom index: 0-19)

1st phase treatment – 'Watchful waiting'. The placebo along with the conservative treatment involving diet management and Pelvic floor exercises were given till such time that there was improvement in the prostatic hyperplasia and/or IPSS/AUA symptom index for benign prostatic hyperplasia which was done at two weeks interval. In case of no improvement, the 2nd phase treatment was given.

Severe intensity (IPSS/AUA symptom index: 19-35)

2nd phase treatment – Four globules, 30 size of 30 C potency of the indicated medicine along with the general management followed by placebo thrice daily was given. A periodic biweekly check-up to assess the progress of the case was done till one year. The indicated medicine was not repeated till improvement lasted. The second prescription depended on the response of the patient to the first prescription as mentioned in Organon of Medicine[13] and Kent's Twelve Observations.[14] The treating physicians were allowed to change the prescription up to three times from among the trial medicines if the first prescription did not work. Only one patient was labeled as clinical failure since he continued to suffer from complaints or worsened after three best indicated medicines have been tried in 30C, 200C and 1000C potencies as per protocol.

As a part of non medical management, patients were advised to urinate when they get the urge, discontinue tobacco, alcohol and caffeine especially after dinner. They were further advised to avoid taking lot of fluid at a time, to avoid decongestant drugs and anti histamines (as these products can increase BPH symptoms), to keep warm and do regular exercise, to reduce stress and to do Kegel/ pelvic floor exercise.

Outcome assessment

The patients were followed up for one year. The outcome assessment of treatment was done by calculating the percentage, using formula (IPSS at entry level minus IPSS after 12 months)/ IPSS at entry level. More than 75% improvement was defined as 'marked improvement', 50 to less than 75% as 'moderate', 25 to less than 50% improvement as 'mild' and less than 25% improvement as 'not significant'. No change in symptom score from base line score after sufficient trial of best indicated medicines was defined as 'not improved' and increase in IPSS as 'worsened'.

Statistical analysis

Data obtained after completion of study was analyzed by paired t test. A two-tailed (α=2) probability (p) value less than 0.05 (p<0.05) was considered to be statistically significant. Analysis was performed on STATISTICA (window version 6.0).

Results

During the period of two years,121 patients were enrolled, out of which 23 did not turn up after baseline investigations, 11 were lost to follow-up, 44 were excluded by Project Monitoring Officers of CCRH due to non adherence of protocol; however these patients were followed-up and data was analyzed separately.

A total of 43 patients completed the study as per protocol during the period. The age of all patients at baseline ranged from 50-80 years with mean (± SE) 65.09 ± 1.23 years. The incidence of benign prostatic hyperplasia was found maximum between 61-70 age group (55.8%), followed by 71-80 age group (27.9%) followed by 50-60 age group (16.3%). The detailed symptoms of patients at base line are given in Table 2.

Table 2: Symptoms of patients at baseline

Symptoms:	No. of Patients	Percentage (%)
Smooth, firm, elastic enlargement of the prostate	43	100.00
Diminished stream	43	100.00
Intermittent voiding	42	97.67
Incomplete emptying	38	88.37
Hesitancy/straining	33	76.74
Post void leakage	10	23.25
Nocturia	42	97.67
Urgency	38	88.37
Retention	00	00.00

The outcome measures of this study are summarized in Table 3. Paired t test for the difference in mean of pre and post treatment IPSS was found statistically significant ($p<0.01$). Difference in mean of pre and post treatment prostate weight and average flow rate also was found statistically significant ($p<0.01$). The pre and post treatment difference in mean of PVRU and Maximum flow rate was found improved but statistically not significant ($p>0.05$). However, the difference in mean of pre and post treatment PSA was found increased, but the PSA levels were maintained with a normal limits (<4.0 ng/ml) in 34 patients.

Table 3: Pre and post treatment status (Mean ± SE, n=43) of different parameters

Outcome measures	Pre treatment	Post treatment	Difference (%)
IPSS (score)	19.63 ± 0.78	100.00	50.29
Prostate weight (gm)	36.34 ± 2.08	100.00	9.80
PVRU (cc)	77.37 ± 11.75	97.67	13.10
PSA (ng/ml)	1.74 ± 0.17	88.37	36.80
Maximum flow (ml/sec)	13.63 ± 1.59	76.74	1.20
Average flow rate (ml/sec)	5.03 ± 0.51	23.25	16.45

ns - ($p>0.05$) ; * - ($p<0.05$) ; ** - ($p<0.01$)

The details of prescribed medicines are summarized in Table 4 which shows that four of the trial medicines were prescribed frequently to the patients (86.0%) suffering from BPH. The medicines were *Lycopodium* (34.9%), *Pulsatilla* (25.5%), *Sulphur* (18.6%) and *Calcarea carb.* (6.9%).

Out of 43 patients, 7 (16.3%) patients showed marked improvement, 14 (32.6%) moderate improvement, 15 (34.9%) mild and 5 (11.6%) not significant improvement while 1 (2.3%) did not improvement and 1 (2.3%) case worsened. Out of 7 patients who showed marked improvement, 1 patient remained on placebo for one year according to phase 1st treatment.

The characteristic indications[12,15] of the medicines found useful are described in Table 5.

Table 4: Prescribed Medicines and their effects (n=43)

Name of medicine(s)	No. of Patient(s)	Improvement Assessment (No. of patients)					
		Marked	Moderate	Mild	Not significant	Not improved	Worsened
Lycopodium	15	2	6	6	1	0	0
Pulsatilla	11	3	2	4	2	0	0
Sulphur	8	0	4	2	2	0	0
Calc. carb.	3	1	1	1	0	0	0
Phosphorus	1	0	1	0	0	0	0
Silicea	1	0	0	1	0	0	0
Thuja	1	0	0	1	0	0	0
Calc. carb., Thuja and Pulsatilla	1	0	0	0	0	1	0
Lycopodium	1	0	0	0	0	0	1
Placeb	1	1	0	0	0	0	0
Total	**43**	**7**	**14**	**15**	**5**	**1**	**1**

Table 5: Characteristic indications of useful medicines

Name of trial medicines	Indications
Lycopodium	Dictatorial; easily angered; anger contradiction from; anger suppressed. Company desire or fond of solitude. Sentimental; consolation aggravates; optimistic, desire sweets; hot patient. Intermittent voiding, nocturia, post void leakage; poor flow of urine, incomplete emptying, hesitancy and urgency before urination.
Pulsatilla	Mildness; sympathetic; emotional; fastidious; offended easily; fear narrow places; consolation ameliorates. Desire company, open air and sweets. Thirstlessness. Hot patient. Intermittent voiding, nocturia, poor flow of urine, incomplete emptying, hesitancy and urgency before urination.
Sulphur	Selfish; reserved; dictatorial; weak memory; nervous temperament; craving for sweets; consolation aggravate; company desires; poor flow of urine; nocturia; urgency and hesitancy before urination; Intermittent voiding; incomplete emptying.

Contd. ...

Contd.

Name of trial medicines	Indications
Calcarea carb.	Chilly patient. Indolence. Obese body built. Profuse perspiration over head. Fear misfortune. Nocturia; post void leakage; hesitancy before urination ; incomplete emptying.
Silicea	Highly chilly patient. Ailments from anxiety. Remorse; consolation aggravate; Nocturia; hesitancy before urination; poor flow of urine and unsatisfactory urination.
Thuja	Reserved; fastidious. Chilly patient. Intermittent voiding; hesitancy before urination; thin and feeble stream of urine; urgency.
Phosphorus	Sympathetic; Contradict disposition; company desire. Craving for cold things. Chilly patient. Intermittent voiding; feeble stream of urine; incomplete emptying and urgency.

The data of patients who were dropped out as they did not follow the protocol guidelines although treated for more than 03 months is given below. Total no. of patients - 30; their mean (± SE) age at entry was 63.43±1.45; the means (± SE) of pre and post treatment IPSS were 20.70±0.83 and 10.20±0.58 respectively. The difference in mean of pre and post treatment was found statistically significant (p<0.01).

Discussion

This was prospective open observational study which has shown positive results in symptom complex and diagnostic laboratory parameters of benign prostatic hyperplasia.

No scientific data is available regarding this type of work in Homoeopathy in which both clinical as well as diagnostic and laboratory parameters have been taken together. In present study, it was observed that the mean (± SE) of IPSS at entry and at end of follow-up was 19.63 ± 0.78 and 9.77 ± 0.74 respectively. The result showed a statistically highly significant decrease of 50.29% in IPSS score. The results supported the hypothesis drawn for the study and thus it could clearly be said that homoeopathic medicines are useful in improving the symptom complex of patients suffering from benign prostatic hyperplasia.

The most useful trial medicines in this study are *Lycopodium, Pulsatilla, Sulphur* and *Calcarea carb.* which are similar to the constitutional medicines used in the previous study by Gupta, et al.[7,8] and *Pulsatilla* by Reddy, et al.[9] But in study by Gupta, et al, organ remedies and mother tinctures were also prescribed to the patients which were not used in the present study. The characteristic symptoms of the medicines used are given in Table 5 which is verified by the present study.

To check the progression of disease was another objective of the study. In this reference, the prostate weight, PVRU and uroflowmetry were the main outcome measures. The mean (± SE) of prostate weight and average flow rate at entry and at the end of study were 36.34 ± 2.08, 32.78 ± 1.74 and 5.03 ± 0.51, 6.02±0.49 respectively. The result showed statistically significant difference in mean values. Similarly the means (± SE) of PVRU and maximum flow rate at entry and at the end of study were 77.37±11.75, 67.22±9.16 and 13.63±1.59, 13.79±1.64 respectively. An assessment of these parameters showed improvement but statistically not significant. The above findings suggest that homoeopathic medicines can check the progression of disease along with improvement of symptom complex in cases of benign prostatic hyperplasia.

PSA is the only parameter which was found increased and the mean (± SE) of pre and post treatment PSA was 1.74 ±0.17 and 2.75 ±0.40 respectively. However, out of 43 patients, PSA remained within normal limits (<4.0 ng/ml) in 34 patients.

One patient (2.3%) remained on placebo for one year which showed improvement in all parameters. Although a very few studies on the natural history of BPH have been reported, but the risk of progression or complications is uncertain. However, in men with

symptomatic BPH, it is clear that progression is not inevitable and some men undergo spontaneous improvement or resolution of their symptoms.[16]

Conclusion

The outcome of this evidence based study is encouraging and will immensely benefit the profession and the aging population at large. These medicines will, therefore, provide a safe and cost effective treatment of BPH.

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References

1. Roehrborn CG, Siami P, Barkin J, et al. The influence of baseline parameters on changes in international prostate symptom score with dutasteride, tamsulosin, and combination therapy among men with symptomatic benign prostatic hyperplasia and an enlarged prostate: 2-year data from the CombAT study. *Eur Urol.* 55, 2009:461–71.
2. Parsons JK, Kashefi C. Physical activity, benign prostatic hyperplasia, and lower urinary tract symptoms. *Eur Urol.* 53, 2008:1228–35.
3. Parsons JK, Carter HB, Partin AW, et al. Metabolic factors associated with benign prostatic hyperplasia. *J Clin Endocrinol Metab.* 91, 2006:2562-2568.
4. Michel MC, Heemann U, Schumacher H, Menlburger L, Goepel M. Association of hypertension with symptoms of benign prostatic hyperplasia. *J Urol.* 172, 2004:1390-1393.
5. Clifford GM, Farmer RD. Drug or symptom-induced depression in men treated with _1-blockers for benign prostatic hyperplasia? A nested case control study. *Pharmacoepidemiol Drug Saf.* 11, 2002:55-61.
6. Chapman Edward. Homeopathy. In Jonas W.B., Levin J.S., Essentials of complementary Medicine, 1999; Lipincott Williams Wilkins (CD ROM).
7. Gupta Girish. Ultrasonographic assessment of Benign Prostate Hypertrophy cases in response to Homoeopathic drugs. *Asian Homoeopathic Journal*. 4(3), 1994:10-17.
8. Gupta Girish, Gupta Naveen, Singh Vijay, Chaudhary Madhu, Singh Mohan. Evidence based study on cases of Benign Prostatic Hyperplasia in response to Homoeopathic drugs. *The Homoeopathic Heritage*. 31(7), 2006: 31 – 41.
9. Reddy GRC, Oberai Praveen, Singh Vikram, Nayak C. Treating Benign Prostatic Hyperplasia in Elderly Men with Homoeopathy- a series of eleven cases. Indian Journal of Research in Homoeopathy. 3(4), 2009:37-40.
10. Barry MJ, Fowler FJJr, O'Leary M P, et al. The American Urological Association symptom index for benign prostatic hyperplasia. *J Urol.* 148, 1992:1549-57.
11. Howard I. Sacher. Hyperplastic and malignant diseases of prostate. In: Braunwald Eugene, Anthony S. Fauci, Dannis L.Kasper, Stephen L. Hauser Dan L. Longo, L. Larry Jameson, editors. Harrison's Principles of Internal Medicine. McGraw-Hill Boston, 2003:608-616.
12. Shah Jawahar. Complete repertory of Hompath Classic (version 8.0); 2006 (CD ROM).
13. Hahnemann Samuel. Organon of medicine, 6th Edition. B. Jain Publishers, New Delhi, 1994.
14. Kent James Tyler. Lectures on Homoeopathic Philosophy. B. Jain Publishers, New Delhi, 2008.
15. Boericke William. Pocket manual of Homoeopathic Materia Medica & Repertory, 9th Edition. B. Jain Publishers. New Delhi, 1994.
16. Joseph C. Presti, et, al. Neoplasms of Prostate gland. In: Emil A. Tanagho, Jack W. Mc Aninch Editors. Smith's General Urology. Mc Graw Hills, New York, 2008:348-374.