*Indian Journal of Research in Homoeopathy*
*Vol. 1, No. 1, 2007*

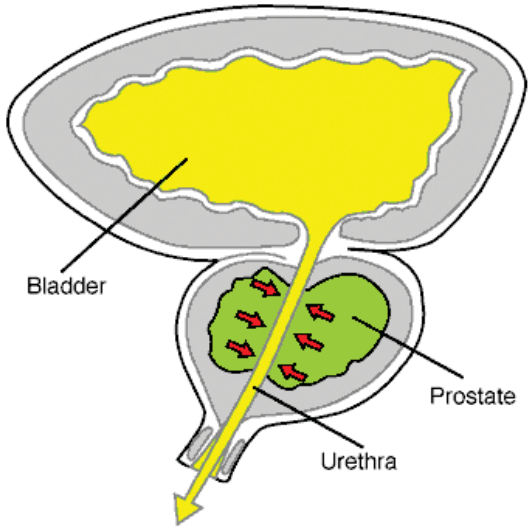
**RESEARCH PROTOCOL**

# A Multicentric Open Clinical Trial to evolve a Group of Efficacious Homoeopathic Medicines in "Benign Prostatic Hyperplasia"

## INTRODUCTION

### A. Literature review

The enlargement of prostate is one of the diseases that affect the old male and if untreated, handicaps him for the rest of his life. From 40 years of age the prostate increases in volume by 2.4 cm cube per year on average. The process begins in the periurethral (central) zone of the prostate and involves both glandular and stromal tissue to a variable degree. Associated symptoms are common from 60 years, and some 50% of men over 80 years of age will have lower urinary tract symptoms associated with benign Prostatic hyperplasia (BPH)[1]. The risk of progression or complications is uncertain. However, in men with symptomatic disease, it is clear that progression is not inevitable and that some men undergo spontaneous improvement or resolution of their symptoms[2].




In Homoeopathy-literature various medicines are given for the treatment of Prostatic enlargement, but no significant work has been done to elicit their efficacy. As such, there is a need to explore the efficacy of homoeopathic medicines otherwise indicated for the various diagnostic symptoms of Benign Prostatic Hyperplasia in the Homoeopathic literature.

### B. Classification:

Benign Prostatic Hyperplasia has been classified in the ICD-10, under item N40, as given below [4]:

N40. **Hyperplasia of prostate:**

- Adenofibromatous hypertrophy of prostate,
- Adenoma (benign) of prostate,
- Enlargement (benign) of prostate,
- Fibroadenoma of prostate,
- Fibroma of prostate,
- Hypertrophy (benign) of prostate,
- Myoma of prostate,
- Median bar (prostate),
- Prostatic obstruction NOS,

**Excludes:** benign neoplasms, except adenoma, fibroma and myoma of prostate.

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### C. Usefulness

The present study plans to evolve a group of efficacious homoeopathic medicines in Benign Prostatic Hyperplasia. It will also define indications of medicines found effective in Benign Prostatic Hyperplasia. This will be a valuable data for indexing in the repertory and the same will immensely benefit the profession and the geriatric patients, at large. These medicines will, therefore, provide a gentle, safe and cost effective treatment of the disease to the ailing geriatric population.

## STUDY OBJECTIVES

### A. Hypothesis

For the open clinical trial, the primary hypothesis is that the use of medicines selected on the basis of repertorisation of the diagnostic signs and symptoms of Benign Prostatic Hyperplasia and its characteristic symptoms, in a single dose, in a specific potency, would be effective in improving the symptom complex of the patient suffering from Benign Prostatic Hyperplasia.

### B. Primary Objective

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

### C. Secondary Objectives

a) To determine and verify the characteristic symptoms of medicine(s) used.

b) To arrest worsening of the disease.

## STUDY DESIGN

### A. Type of Study:

A prospective, multicenter, open, clinical trial.

### B. Approach:

The study is designed to prove or disprove the hypothesis stated above. This is conditional on each study centre adhering to the protocol, ensuring quality control and minimizing loss to follow-up to below 5% and is also subject to the fact that the studies continue till adequate sample size of each drug is recruited.

### C. Location:

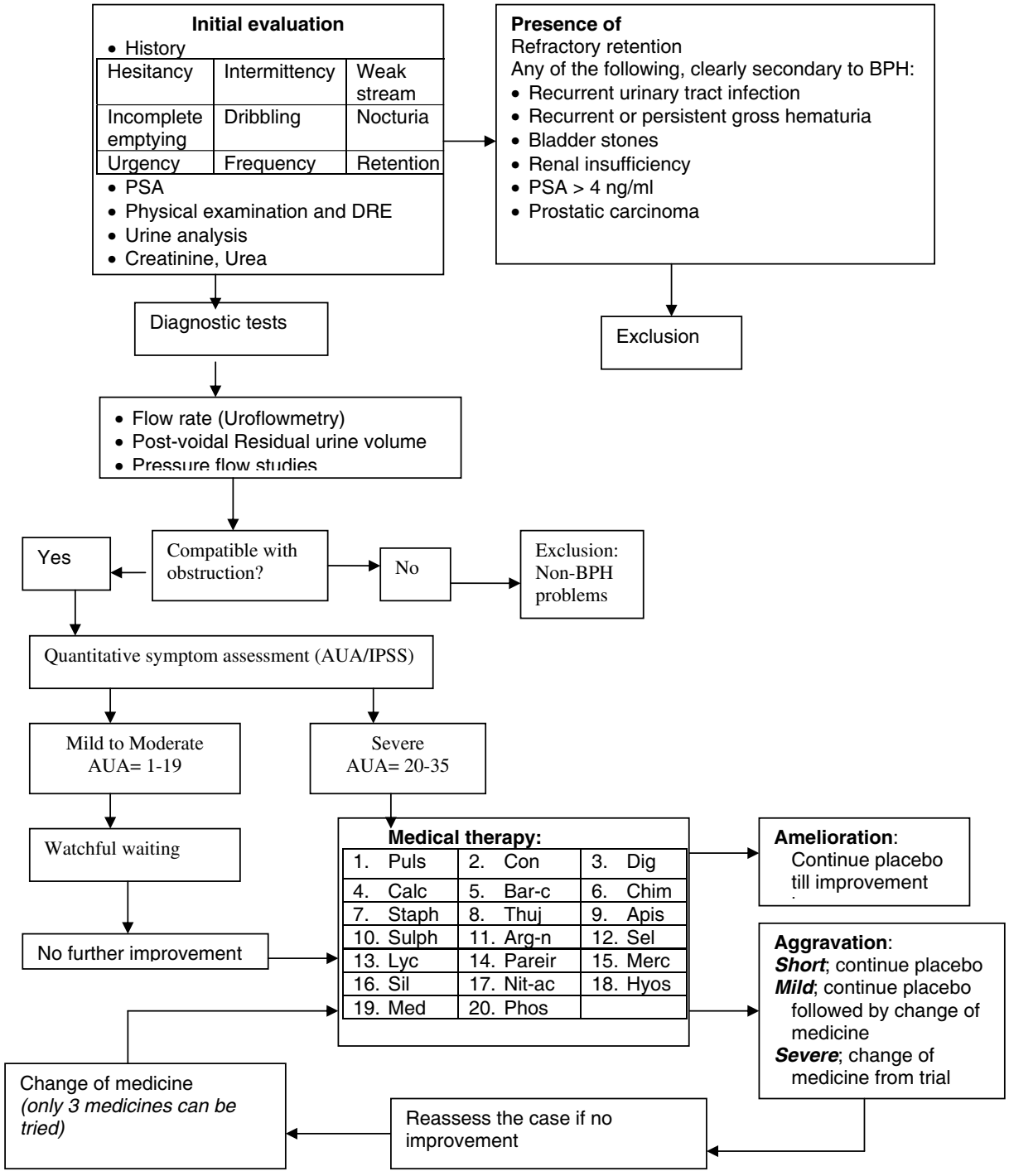
The Institutes/Units under the Council with adequate manpower, Laboratory facilities and research personnel willing to carry out the research study have been selected.

### D. Duration of Study:

3 years.

## E. Study Design (in details):

### BHP Protocol design diagram



## DIAGNOSIS (Benign Hyperplasia of Prostate) [2]

### A. Symptoms

- Hesitancy in initiating voiding
- Intermittent voiding
- Diminished stream
- Incomplete emptying
- Post void leakage
- Nocturia
- Urgency
- Urinary retention

### B. Signs

- Prostate enlargement, consistency*:* smooth/ firm / elastic.
  *(On digital rectal examination)*

### C. Investigations

- Prostate Specific Antigen (PSA*) titer d" 4 ng/ml
- Ultra sound (prostate weight <20 gm; increased residual urine)
- Urine examination for blood or infection: negative
- Transrectal ultrasound
- IVP with post voided film
- Renal function test
- Uroflowmetry

*PSA is to be done prior to, and not after, the Digital Rectal Examination or the Transrectal Ultrasound.

*Ultrasound, PSA level and Uroflowmetry are normally to be done at entry, after 3 months and after 1 year. If needed, these investigations may be carried out more frequently.*

### Inclusion criteria:

- People of 50 years and above with signs and symptoms of Benign Hyperplasia of Prostate.
- On ultrasound examination: a swollen or enlarged prostate (more than 20g).

### Exclusion criteria:

- Prostate Specific Antigen titer > 4 ng/ml
- Prostate weight <20 gm
- Urine examination for presence of blood or infection
- On Digital rectal examination presence of hard, lumpy, or abnormal areas in the enlarged prostate.
- Complete retention of urine for more than 24 hours.
- During treatment, marked fluctuation of or increase in the PSA level
- Benign neoplasms, except adenoma, fibroma and myoma of prostate.
- Prostatic carcinoma,
- Other possible causes of the symptoms, such as Urinary tract infection, neurogenic bladder, or urethral stricture.

## STATISTICAL PLAN

### A. Sample size:

- 600 cases. (Keeping also a margin for the drop out cases).
  *369 cases will be sufficient to assess the outcome of improvement rate of 60% with absolute error of +5% and with a confidence level of 95%.*

### B. Statistical analysis

Data obtained during the study would be analyzed by t' test statistical methods.

## PROCEDURE OF SELECTION OF MEDICINE

### A. Selection of the drugs:

The selection of the drugs has been arrived at by repertorising the symptoms of the Benign Prostatic Hyperplasia (BPH) using the Complete Repertory[5] 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 Repertory have been short-listed along with the prescribing characteristic symptoms (Physical/Mental Generals) of each of these drugs.

### B. Rubrics taken up for repertorization:

| **BENIGN PROSTATIC HYPERPLASIA** | | | |
|---|---|---|---|
| | **Symptom** | **Corresponding Rubric in the Complete Repertory[5]** | |
| 1 | Smooth, firm, elastic enlargement of the prostate | **PROSTATE** | 1a **SWELLING** |
| | | | 1b **ENLARGEMENT** |
| 2 | Hesitancy/straining | | 2a retarded, must wait for urine to start |
| | | | 2b retarded, must wait for urine to start; press, must; prostate affections, in |
| | | | 2c retarded, must wait for urine to start; press, must; a long time before he can begin |
| 3 | Intermittent voiding | | 3a interrupted, intermittent |
| | | | 3b spurting stream |
| | | | 3c interrupted, intermittent; spurts, in swelled prostate, with each spurt cutting pain |
| 4 | A diminished stream | BLADDER; URINATION | 4a thin stream |
| | | | 4b feeble stream, slow, weak |
| 5 | Incomplete emptying | | 5a unsatisfactory |
| | | | 5b unsatisfactory; feeling as if urine remained in urethra |
| 6 | Post void leakage | | 6a dribbling by drops; enlarged prostate, with |
| | | | 6b dribbling by drops; urination, after |
| | | | 6c unsatisfactory; bladder were not emptied, as if, with dribbling |
| 7 | Nocturia | | 7a frequent; night |
| | | | 7b frequent; old people; enlarged prostate, with |
| | | | 7c frequent; prostate affections, with |
| 8 | Urgency | BLADDER; URGING to urinate | 8 morbid desire; sudden; hasten to urinate, must, or urine will escape |
| 9 | Retention | BLADDER; RETENTION of urine | 9 enlarged prostate, from |

## C. Short listed remedies consequent upon Repertorisation [5]:

| | Puls | Con | Dig | Calc | Bar-c | Chim | Staph | Thuj | Apis | Sulph | Arg-n | Sel | Lyc | Pareir | Merc | Sil | Nit-ac | Hyos | Med | Phos |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 26/13 | 17/09 | 17/09 | 12/05 | 10/05 | 11/06 | 23/14 | 22/13 | 18/11 | 18/08 | 16/10 | 15/09 | 14/08 | 13/09 | 13/06 | 12/08 | 12/06 | 11/06 | 10/06 | 09/07 |
| **1a** | **2** | **2** | **2** | **0** | **0** | **3** | **1** | **1** | **0** | **0** | **0** | **1** | **0** | **0** | **0** | **0** | **0** | **0** | **1** | **0** |
| **1b** | **3** | **3** | **3** | **3** | **3** | **2** | **2** | **2** | **2** | **2** | **2** | **2** | **2** | **2** | **2** | **2** | **2** | **2** | **2** | **2** |
| | **21/11** | **12/07** | **12/07** | **09/04** | **07/04** | **06/04** | **20/12** | **19/11** | **16/10** | **16/07** | **13/08** | **12/07** | **12/07** | **11/08** | **11/05** | **09/06** | **10/05** | **09/05** | **07/04** | **07/06** |
| 2a | 1 | 0 | 2 | 1 | 0 | 0 | 1 | 2 | 2 | 1 | 1 | 2 | 3 | 2 | 0 | 2 | 2 | 0 | 1 | 0 |
| 2b | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2c | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 1 | 2 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 2 | 2 | 0 | 0 |
| 3a | 2 | 3 | 0 | 0 | 0 | 0 | 0 | 2 | 1 | 2 | 1 | 0 | 2 | 1 | 0 | 0 | 0 | 0 | 1 | 1 |
| 3b | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 3c | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 4a | 2 | 0 | 0 | 0 | 0 | 1 | 2 | 2 | 1 | 2 | 0 | 0 | 0 | 0 | 2 | 0 | 2 | 0 | 0 | 0 |
| 4b | 1 | 0 | 2 | 0 | 0 | 1 | 1 | 1 | 2 | 3 | 3 | 2 | 1 | 1 | 3 | 1 | 2 | 0 | 2 | 1 |
| 5a | 1 | 1 | 0 | 2 | 0 | 0 | 2 | 2 | 0 | 2 | 2 | 2 | 1 | 0 | 1 | 1 | 0 | 2 | 0 | 1 |
| 5b | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 2 | 0 | 0 | 2 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| 6a | 2 | 0 | 2 | 0 | 1 | 0 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| 6b | 0 | 2 | 1 | 3 | 2 | 0 | 2 | 2 | 0 | 0 | 1 | 2 | 1 | 2 | 0 | 1 | 0 | 0 | 0 | 1 |
| 6c | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 7a | 3 | 2 | 1 | 3 | 3 | 0 | 1 | 2 | 2 | 3 | 1 | 1 | 3 | 0 | 3 | 3 | 2 | 2 | 3 | 1 |
| 7b | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 7c | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 8 | 3 | 0 | 0 | 0 | 1 | 0 | 1 | 2 | 2 | 3 | 2 | 0 | 0 | 2 | 2 | 0 | 0 | 2 | 0 | 2 |
| 9 | 2 | 1 | 3 | 0 | 0 | 2 | 3 | 0 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 |

## D. Trial medicines

| | | | |
|---|---|---|---|
| 1. Pulsatilla | 2. Conium mac. | 3. Digitalis | 4. Calcarea carb. |
| 5. Baryta carb. | 6. Chimaphilla | 7. Staphysagria | 8. Thuja |
| 9. Apis mel. | 10. Sulphur | 11. Argentum nitricum | 12. Selenium |
| 13. Lycopodium | 14. Pareira brava | 15. Merc. sol. | 16. Silicea |
| 17. Nitric acid | 18. Hyoscyamus | 19. Medorrhinum | 20. Phosphorus |

## E. Selection of Medicine

Selection of medicine is to be made out of the 20 medicines taken up for clinical trial. The first prescription from amongst these 20 medicines shall be the one that fetches the highest value on repertorisation of the presenting signs and symptoms of the disease in a particular subject and its selection shall be further guided by the characteristic mental/emotional and physical attributes of the patient and concomitant(s), if any.

*Cases which need medicine(s) other than the trial group of medicines may be treated separately by the indicated medicine but these subjects will not be included in the study. A separate record of such cases is however to be maintained at the center.*

## F. Potency:

30C.

### G. Dose

4 pills. *(Globule size 30).*

### H. Repetition

Single dose of indicated medicine will be given and this will not be repeated [6] [7].

### I. Follow up (Change of Medicine / Second Prescription)

| | RESPONSE | FOLLOW-UP (1-2 wks) STATUS | ACTION |
|---|---|---|---|
| 1 | Amelioration | Continuous improvement | Placebo so long as improvement continues |
| 1a | | improvement ceases | Repeat single dose of the next higher potency of the same medicine |
| 2 | Amelioration | *with* reappearance of old symptoms | Placebo to continue |
| 2a | Static | Old symptoms *persist* | Repeat single dose of the next higher potency of the same medicine |
| 3 | Homoeopathic aggravation | Short aggravation followed by prolonged amelioration | Placebo so long as improvement continues |
| 3a | Aggravation not followed by amelioration | Intensity: mild | Wait for a week; follow with change of medicine in static or worsening state |
| 3b | | Intensity: severe | Repeat single dose of the next higher potency of the changed medicine |
| 4 | Appearance of new symptoms | Intensity: mild | Wait for a week with Placebo |
| 4a | | Static or worse after a week | Change of medicine (next best trial medicine) |
| 4b | | Intensity: severe | The changed medicine in the next higher potency |
| 5 | No change after 1 week of indicated medicine | | Repeat in higher potency (2C/1M) |
| 6 | No change in spite of raising the potency | | Change of medicine, after removing obstacles, if any |
| 7 | No relief in spite of using three indicated trial medicines | | The case to be closed and labeled as Clinical failure |

### J. Source of Trial Medicines:

Homoeopathic medicines for the trial in different study centers should be of the same batch number procured from a single pharmacy.

### K. General supportive care or Non Medicinal Management:

To advise the patient as follows:

1. Not to hold but void soon on the urge to urinate.

2. To discontinue tobacco.
3. To avoid alcohol and caffeine, especially after dinner.
4. To drink little fluid at a time, spread out throughout the day and avoid them within two hours of bedtime.
5. To avoid cold and sinus medications that contains decongestants and antihistamines. These medications can increase BPH symptoms.
6. To keep warm and exercise regularly. Cold weather and lack of physical activity may worsen symptoms.
7. To reduce stress. Nervousness and tension can lead to more frequent urination.
8. To perform *Kegel/Pelvic strengthening exercises*.

## L. Plan of treatment

To be based on the severity of the discomfort determined by the AUA/International Prostate Symptom Score (IPSS) assessment.

**IPSS / AUA Symptom Score**

| | | | (Circle one number on Each Line) | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | 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 |
| **Over the past month, how often,** | Have you had a sensation of not empty your bladder completely after you finish urinating? | *Incomplete emptying | 0 | 1 | 2 | 3 | 4 | 5 |
| | Have you had to urinate again less than 2 h after you finished urinating? | **Frequency | 0 | 1 | 2 | 3 | 4 | 5 |
| | Have you found you stopped and started again several times when you urinated? | *Intermittency | 0 | 1 | 2 | 3 | 4 | 5 |
| | Have you found it difficult to postpone urination? | **Urgency | 0 | 1 | 2 | 3 | 4 | 5 |
| | Have you had a weak urinary stream? | *Weak stream | 0 | 1 | 2 | 3 | 4 | 5 |
| | Have you had to push or strain to begin urination? | *Straining | 0 | 1 | 2 | 3 | 4 | 5 |
| | 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? | **Nocturia (times per night) | 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)*

*Obstructive symptoms due to Benign proliferative disease of the Prostate.

** *Secondary irritative symptoms from reduced bladder compliance consequent upon the resistance to urine flow.*

**I. Mild to moderate intensity *(IPSS score: 0-19)***

***1st phase treatment*** – "Watchful waiting". The placebo along with the conservative treatment (Non-medicinal management) involving diet management and Pelvic floor exercises to be carried out till such time that there is improvement in the prostatic hyperplasia and/or the International Prostate Symptoms Score (IPSS) or The American Urological Association (AUA) symptom index for benign prostatic hyperplasia, which shall be done at two week's interval. In case of no improvement, the 2nd phase treatment will be given.

***2nd phase Treatment*** – The indicated medicine along with the general management, to be followed by a periodic check-up to assess the progress in the case.

**II. Severe intensity *(IPSS score: 19-35 )***

***Only 2nd phase Treatment***- The general management and the indicated medicine together, to be advised straight away since the intensity of complaints warrants an immediate relief in the discomfort.

## PROCEDURES AND METHODS

### A. Enrolment of subjects:

The enrolment of the subjects for the study consists of four stages…

Stage 1: *Preliminary verbal screening* by the OPD doctor for presence of inclusion criteria

Stage 2: *Detailed screening* by the investigating officer for presence of inclusion criteria and absence of all exclusion criteria

Stage 3: *Informed written consent* of potentially eligible subjects

Stage 4: *Baseline assessment* of subjects who clear 'Stage 3'.

### B. Selection of medicine out of the 20 trial medicines:

**1. The rubrics corresponding to the symptoms of BPH in the subject are selected:**

| | Tick the rubric(s) found in the case | No | ✓ |
|---|---|---|---|
| 2a | URINATION; retarded, must wait for urine to start | 1 | |
| 2b | URINATION; retarded, must wait for urine to start; press, must; prostate affections, in | 2 | |
| 2c | URINATION; retarded, must wait for urine to start; press, must; a long time before he can begin | 3 | |
| 3a | URINATION; interrupted, intermittent 4 | | |
| 3b | URINATION; spurting stream | 5 | |
| 3c | URINATION; interrupted, intermittent; spurts, in swelled prostate, with each spurt cutting pain | 6 | |
| 4a | URINATION; thin stream | 7 | |
| 4b | URINATION; feeble stream, slow, weak | 8 | |
| 5a | URINATION; unsatisfactory | 9 | |
| 5b | URINATION; unsatisfactory; feeling as if urine remained in urethra | 10 | |
| 6a | URINATION; dribbling by drops; enlarged prostate, with | 11 | |
| 6b | URINATION; dribbling by drops; urination, after | 12 | |
| 6c | URINATION; unsatisfactory; bladder were not emptied, as if, with dribbling | 13 | |
| 7a | URINATION; frequent; night | 14 | |
| 7b | URINATION; frequent; old people; enlarged prostate, with 157cURINATION; frequent; prostate affections, with 16 | | |
| 8 | URGING to urinate, morbid desire; sudden; hasten to urinate, must, or urine will escape | 17 | |
| 9 | RETENTION of urine; enlarged prostate, from | 18 | |

**2. The selected rubrics are then repertorised:**

**Highlight the row(s) below corresponding to the rubric no(s). ticked above:**

| Total | Puls | Con | Dig | Calc | Bar-c | Chim | Staph | Thuj | Apis | Sulph | Arg-n | Sel | Lyc | Pareir | Merc | Sil | Nit-ac | Hyos | Med | Phos |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2a | 1 | 0 | 2 | 1 | 0 | 0 | 1 | 2 | 2 | 1 | 1 | 2 | 3 | 2 | 0 | 2 | 2 | 0 | 1 | 0 |
| 2b | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2c | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 1 | 2 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 2 | 2 | 0 | 0 |
| 3a | 2 | 3 | 0 | 0 | 0 | 0 | 0 | 2 | 1 | 2 | 1 | 0 | 2 | 1 | 0 | 0 | 0 | 0 | 1 | 1 |
| 3b | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 3c | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 4a | 2 | 0 | 0 | 0 | 0 | 1 | 2 | 2 | 1 | 2 | 0 | 0 | 0 | 0 | 2 | 0 | 2 | 0 | 0 | 0 |
| 4b | 1 | 0 | 2 | 0 | 0 | 1 | 1 | 1 | 2 | 3 | 3 | 2 | 1 | 1 | 3 | 1 | 2 | 0 | 2 | 1 |
| 5a | 1 | 1 | 0 | 2 | 0 | 0 | 2 | 2 | 0 | 2 | 2 | 2 | 1 | 0 | 1 | 1 | 0 | 2 | 0 | 1 |
| 5b | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 2 | 0 | 0 | 2 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| 6a | 2 | 0 | 2 | 0 | 1 | 0 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| 6b | 0 | 2 | 1 | 3 | 2 | 0 | 2 | 2 | 0 | 0 | 1 | 2 | 1 | 2 | 0 | 1 | 0 | 0 | 0 | 1 |
| 6c | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 7a | 3 | 2 | 1 | 3 | 3 | 0 | 1 | 2 | 2 | 3 | 1 | 1 | 3 | 0 | 3 | 3 | 2 | 2 | 3 | 1 |
| 7b | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 7c | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 8 | 3 | 0 | 0 | 0 | 1 | 0 | 1 | 2 | 2 | 3 | 2 | 0 | 0 | 2 | 2 | 0 | 0 | 2 | 0 | 2 |
| 9 | 2 | 1 | 3 | 0 | 0 | 2 | 3 | 0 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 |

**3. The medicines with highest value are recorded below:**

| | | | | |
|---|---|---|---|---|
| High scoring medicines: | | | | |
| Medicine: | _____ | _____ | _____ | _____ |
| Value: | ___/___ | ___/___ | ___/___ | ___/___ |

**4. One medicine out of this high scoring trial medicine is selected on the basis of characteristic symptom similarity:**

**Basis of prescription**

| **Prescription: _____** | **Potency: 30. Dose: single** | |
|---|---|---|
| **Highlight the disease symptom(s) of the case** | **No.** | **State the characteristic symptom(s) of selected medicine** |
| retarded, must wait for urine to start | 1 | |
| retarded, must wait for urine to start; press, must; prostate affections, in | 2 | |
| retarded, must wait for urine to start; press, must; a long time before he can begin | 3 | |
| interrupted, intermittent | 4 | |
| spurting stream | 5 | |
| interrupted, intermittent; spurts, in swelled prostate, with each spurt cutting pain | 6 | |

| | | |
|---|---|---|
| thin stream | 7 | |
| feeble stream, slow, weak | 8 | |
| unsatisfactory | 9 | |
| unsatisfactory; feeling as if urine remained in urethra | 10 | |
| dribbling by drops; enlarged prostate, with | 11 | |
| dribbling by drops; urination, after | 12 | |
| unsatisfactory; bladder were not emptied, as if, with dribbling | 13 | |
| frequent; night | 14 | |
| frequent; old people; enlarged prostate, with | 15 | |
| frequent; prostate affections, with | 16 | |
| URGING to urinate, morbid desire; sudden; hasten to urinate, must, or urine will escape | 17 | |
| RETENTION of urine; enlarged prostate, from | 18 | |

### C. Assessment:

#### 1. Periodical – two-weekly

The "zero" will be the time of enrollment. The study personnel will call the patient every two weeks or earlier, if need be, for the follow-up visit and will examine the patient. All the patients will be taught to recognize the signs of worsening illness according to those outlined in Baseline assessment form. They will be advised to report to the Institute if any of the signs develop at any time before the scheduled visit. The following observation will be made and recorded in case report forms:

1. Change in Prostate enlargement by DRE
2. Change in IPSS/AUA score
3. Presence or absence of Urinary tract infection
4. Signs of very severe disease.
5. Number of doses of medicines taken.
6. If the patient does not report on a date (fixed) effort shall be made to contact him/her in any way.

The investigator should attempt to establish the severity of exacerbation as well as the severity of pre-existing disease condition.

#### 2. Outcome assessment

On each follow-up visit an assessment of clinical success or failure shall be made depending upon an overall response to treatment.

#### 3. Treatment Assessment

Assessment will be done either after all the potencies (30, 200 and 1M) of the trial drug have been used or after a lapse of a term of 3 months from enrollment of the patient whichever be earlier. Patients who get clinically improved or achieve an IPSS Score '0', will be discontinued from therapy and put on periodic observation for a symptom-free period up to one year. Those who are not improved will be given a changed therapy after a wash-out period of two weeks, following the same guidelines as for the

selection of the first prescription and this case shall be taken as a new trial medicine subject in the study.

**i. Assessment of *improvement*-**

1. *Marked ( more than 75% improvement in IPSS Symptom score from Base line score)
2. *Moderate ( 50% to less than 75% improvement in IPSS Symptom score from Base line score)
3. *Mild ( 25% to less than 50% improvement in IPSS Symptom score from Base line score)
4. Not Significant ( less than 25% improvement in IPSS Symptom score from Base line score)
5. Not Improved ( No change in Symptom score from IPSS Base line score after sufficient trial of best indicated medicines )
6. Worsened (Increase in IPSS Score)
7. Static (No change of IPSS Score from Baseline)
8. Referred: Referred for other therapy in the eventuality of any adverse event
9. Withdrawal: Subject withdraws consent or refuses for further treatment
10. Drop out: Does not fulfill the conditions as per protocol

**ii. Group of efficacious Homoeopathic medicines**

**iii. Characteristic symptoms (P, Q, R, S) of Homeopathic medicines found effective.**

**iv. Clinical symptoms of Homoeopathic medicines found effective**

**v. Improvement %age:**

$$\text{* \% of improvement} = \frac{\text{Total score at entry level} - \text{Total score on completion of study}}{\text{Total score at entry level}} \times 100$$

## CRITERIA FOR WITHDRAWAL OF PATIENTS

### A. When to withdraw the subject

It is the responsibility of the center investigator to maintain the subject in the study, provided it is safe to do so. A subject may be discontinued from the study for any of the following reasons, *which must be documented:*

**1. Clinical failure:**

i. No change in the symptom picture of the subject after the trial is complete. i.e. when none of the three indicated trial medicines show any improvement.

**2. Occurrence of a serious adverse event (defined):**

i. Persistent increase in symptom score from baseline assessment score.
ii. Serious undercurrent illness.

**3. Patient withdraws consent**

**4. Protocol is not followed**

## MONITORING AND INSPECTION

### A. Project Monitoring and reviews :

i. Site visits**:** Site visits will be made by the monitoring officer from CCRH Headquarter between 3-6 months after commencement of studies.

ii. Presentation of interim data by the center investigator will be made at Headquarter.

iii. Data review board (DRB) will monitor the information with respect to deviations from the study protocol, in appropriate enrolment of study subject, missed observations etc. and will suggest plan to rectify any problems at the site.

## ETHICAL REVIEW

Although Homoeopathic medicines, proposed to be used during the study, are homoeopathic pharmacopoeal preparations (no new drug is proposed to be tried) yet necessary Clearance of the Institutional Ethical Committee should be obtained before undertaking the study.

**Note:**

i. *This Protocol may be used by other individuals / institutes as well. The full version of the protocol can be had from the Council for this purpose.*

ii. *The Council will be grateful if the outcome assessment of study(s) conducted by the Investigator(s) as per Protocol guidelines is communicated prospectively to further validate the efficacy of pre-selected homoeopathic medicines in Benign Prostatic Hyperplasia.*

## BIBILIOGRAPHY

1. Haslett, Christopher, et al. *Davidson's Principles and Practice of Medicine,* Churchill Livingstone, 19th Edition 2002; 13:508-636,637.
2. Eugene Braunwald, et al. *Harrison's Principals of Internal Medicine,* Volume II, *McGraw-Hill,* Medical Publishing Division, 15th Edition 2001; 258:608-609..
3. W.H.O., ICD-10, *International Statistical Classification of Diseases and Related Health Problems,* Volume 1, World Health Organization, Geneva, Tenth Revision 1992; J40-J47: 697.
4. Swash Michael. *Hutchison's Clinical Methods, W.B. Saunders,* 21st Edition 2002; 5:150-151
5. *Complete Repertory* 3.0.(English) 5.1 Repertory by Roger van Zandvoort, MacRepertory for Windows, Kent Homoepathic Associates, USA.
6. Dubey S.K., *Text Book of Materia Medica*
7. Hahnemann, Samuel. *Organon of medicine.* 5th & 6th edition.
8. Sarkar B.K.. Organon of medicine - Commentary, M. Bhattacharyya & Co. (P) Ltd., Calcutta 1980, P-238-253.