ORIGINAL ARTICLE

Bacopa monnieri - A multicentric, randomized, double-blind homoeopathic pathogenetic trial

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***Objective*:** To elicit the pathogenetic response of the drug Bacopa monnieri in homoeopathic potencies on healthy human beings.

Methodology: Drug *Bacopa* monnieri was proved by the Central Council for Research in Homoeopathy through randomized, double-blind, placebo-controlled method. The study was conducted at two centers. The drug was proved in three potencies (6C, 30C and 200C) on 32 apparently healthy volunteers who were selected after conducting pre-trial medical examination by the medical specialists and routine laboratory investigations. In the first phase volunteers were given 56 doses (04 doses per day for 14 days) of placebo. In the next three phases 56 doses (04 doses per day for 14 days) of each potency or placebo were consumed. The symptoms generated during the trial period were noted by the volunteers and elaborated by the Proving Masters. The data obtained from both the centers was compiled at proving-cum-data processing cell at CCRH headquarters after de-coding.

Observations: Out of the 20 provers who were on actual drug trial, 07 manifested symptoms. Drug was able to produce symptoms in all three potencies more or less related to every part of the body.

Conclusion: The pathogenetic responses elicited during the proving trial expands the scope of use of the drug *Bacopa* monnieri and will benefit the research scholars and clinicians. These symptoms will carry more value when verified clinically.

Keywords: homoeopathy; pathogenetic effect; homoeopathic pathogenetic trial; drug proving; *Bacopa* monnieri

INTRODUCTION

This is an annual creeping plant, found in moist places near streams or on the border of tanks throughout India.[1,2] Leaves are tiny and thick. Flowers are white, sometimes slightly bluish in colour, appearing in spring and summer. Taste of the plant is slightly bitter.[1] The root as well as the stalks and leaves are used in the Hindu medicine. It is considered to be a nerve tonic, and useful in insanity and epilepsy.[2]

It is also useful in asthma and hoarseness. Stem and leaves are used in snake bite.[3] Leaves are used as a diuretic and aperient.[4] Standardized Bacopa monnier extract is efficacious in subjects with age-associated memory impairment with significant improvement on mental control, logical memory and impaired associated learning.[5] The studies provide further evidence that Bacopa monnieri has potential for safely enhancing cognitive performance in aging.[6] Bacopa monnieri has been used in the Ayurvedic system of medicine for centuries. The methanol extracts of the plant were found to have potent antioxidant, antimicrobial and anti-inflammatory properties. These active crude methanol extracts were also assayed for cellular toxicity to fresh sheep erythrocytes and found to have no cellular toxicity.[7]

The alkaloid obtained from H. monniera for which the name 'brahmine' is suggested, has been studied by Bose and Bose (1931). They find that it is highly toxic. Frogs are killed within 10 minutes with a dose of 0.5 mg. per 100 gm. body weight. Rats and guinea pigs

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are killed within 24 hours with a dose of 25 mg. per kilo body weight. A dose of 0.5 mg. per kilo body weight of cat produces a fall of blood pressure. In smaller doses, however, there is a slight rise of blood pressure due to vaso-constriction and stimulation of the cardiac muscles. The respiration is stimulated in small doses. Plain muscles like that of the small intestines, uterus, etc., are stimulated in dilutions of 1 in 2,00,000 to 1 in 5,00,000. In therapeutic doses, the alkaloid resembles strychnine in action. Bose has used powdered dried leaves of the Brahmi plant with very satisfactory results in cases of asthenia, nervous breakdown and other run-down conditions.[2]

No literature related to homoeopathic proving of Bacopa monnieri was found. Therefore, a systematic Homoeopathic Pathogenetic Trial (HPT) of the drug in homoeopathic potencies was necessary to elicit its pathogenetic power which was carried out by Central Council for Research in Homoeopathy as per its approved protocol.

Botanical Name[3] : Bacopa monnieri (Linn.) Pennell

Synonym[3] : Herpestis monniera (Linn.) H.B. & K., B. monniera Wettst. Moniera cuneifolia Michx.

Family[8] : Scrophulariaceæ

Common names3,8:

Hindi	:	Brahmi, Barami
Sanskrit	:	Brahmi
Bengali	:	Brihmi-sak
Kannad	:	Nirubrahmi
Tamil	:	Nirpirami
Malayalam	:	Nirbrahmi
Telugu	:	Sambrani chettu
Marathi	:	Jalnaveri
English	:	Thyme-leaved Gratiola

Description

A small, glabrous, somewhat succulent creeping herb, rooting at the nodes, with branches 10 to 35 cm long, creeping and ascending. Leaves 6 to 25 mm by 2.5 to 10 mm, sessile, opposite, decussate, obovate-oblong or spatulate, rather fleshy, very obtuse. Flowers axillary, solitary, bluish-white or yellowish, bracteolate, pedicels long, slender. Bracteoles [2], linear, just adjacent to calyx; calyx 2+3, outer[2] broad, long, 5 to 7 X 2 to 33 mm; inner [3], short, linear, about 1 to 2 mm broad; corola [5], gamopetalous, bluish-white, yellowish, 8 mm long, lobes sub equal, upper[3] long, broad than lower[2], all with shining dots; stamens didynamous, included; style dilated at the top, 2-lobed or entire. Fruit a capsule, ovoid, acute, [2] grooved.[9]

Distribution

Throughout India in wet, damp and marshy areas.[3]

Part used in Homoeopathy

Whole plant.[9]

Potencies used

6C, 30C & 200C

Objective

To elicit the pathogenetic response of the drug Bacopa monnieri on apparently healthy human volunteers in homoeopathic potencies.

MATERIALS AND METHODS

Study Design

The study was a randomized, double-blind, placebo controlled trial.

Location and duration of study

The proving was conducted at Drug Proving Research Unit (Homoeopathy), Midnapore and in Drug Proving Research Unit (Homoeopathy), Kolkata from 2005-06.

Participants

Total 32 apparently healthy volunteers from above mentioned centers, between the age group of 18 to 50 years, comprising of 29 males and 03 females, were enrolled in this study. Pre-trial Medical Examination (PME) and Terminal Medical Examination (TME) of the volunteers were carried out by General Physicians, Psychiatrists, Cardiologists, Ophthalmologists, ENT Specialists, Dermatologists, Gynaecologists, Radiologists and their routine laboratory investigations at the centers were done to ascertain their health status. After recommendation of experts, healthy volunteers were enrolled in the Homoeopathic Drug Proving Programme.

'Written informed consent' from each volunteer was obtained before starting the proving. PME was conducted to confirm health status of the volunteers. Volunteers declared healthy, were enrolled in the study. The study was conducted at two centers. Out of total

32 volunteers, 20 were kept on drug (verum) and 12 were on placebo (control) in all four phases. All the volunteers were assigned code numbers and the coded drugs of different potencies (including placebo) which were supplied in separate glass phials bearing code numbers of the respective volunteers; keeping both provers and proving masters blind about what provers were consuming (drug or placebo).

Drug

Bacopa monnieri was procured in 6C, 30C and 200C potencies from M/s. Dr. Willmar Schwabe India Pvt. Ltd., NOIDA, in 100 ml. sealed phials of each dilution. Globules (number 30) were medicated with these attenuations at the Council's headquarters office and sent to Drug Proving Research Units in coded phials (verum) along with placebo (control).

Placebo

Placebo was made up of unmedicated globules (number 30) moistened with unmedicated dispensing alcohol (unsuccussed) and was therefore indistinguishable from verum.

Procedure of proving

Before commencing the study, all volunteers were screened strictly by the experts and apparently healthy provers between the age group of 18-50 years, both males and females were included in the drug proving trial. Pregnant and lactating mothers were excluded.

The study consisted of four phases. Each phase consisted of 56 doses of drug or placebo.

Phase-I : Placebo phase. It is useful in generating prover's response to placebo and therefore symptoms generated by the prover in this stage act as control for subsequent phases.

Phase-II : In 2nd phase, the proving was conducted with 6C potency.

Phase-III : In 3rd phase, the proving was conducted with 30C potency.

Phase-IV : In 4th phase, the proving was conducted with 200C potency.

The volunteers were asked to take 4-6 globules of a particular potency of the coded drug, four times a day, dry on tongue.

They were instructed to note down the details of their feelings/changes in mind and body, after taking the coded drug/placebo in 'Prover's Day Book Proforma' daily.

- *If symptoms(s)/sign(s) appeared*

The volunteers were asked to stop taking the drug/placebo as soon as any symptom(s)/sign(s) developed during the trial.

The volunteer noted down the sequence of the appearance of new sign(s) and/or symptoms(s), their progress and the number of doses after which such sign(s) and/or symptoms(s) appeared with date, time of onset and duration for which they persisted. Intake of drug remained suspended till the sign(s) and/or symptoms(s) totally disappeared. Any change in normal routine of the prover in respect of daily habits pertaining to diet, living conditions etc./any treatment taken was also noted in the Prover's Day Book Proforma.

After disappearance of symptom(s) and/or sign(s) produced by the drug, the volunteer had to wait for a further period of 07 days before taking the remaining doses of that potency following the same dose schedule as stated above. In case of further appearance of new sign(s) and/or symptom(s), the same procedure as stated above was followed till the consumption of 56 doses of that potency by the volunteer.

If the prover was experiencing the same symptom(s) what he/she had already shown, he/she was asked to stop the current quota and to switch over to the next quota after a washout period of 14 days.

Each prover was interrogated everyday by Proving Master about the appearance of new symptom(s) or progress of symptoms and noted those in 'Symptom Elaboration Proforma' with respect to appearance and dis-appearance of symptoms, their location, sensation/character, modalities, concomitants, extension of symptoms, causation, clinico-pathological findings

- If no symptoms(s)/sign(s) appeared

The volunteers noted down as 'No Symptom' with date and time of intake of the respective dose of the drug/placebo.

Before commencing the administration of subsequent potencies (subsequent phase) of the drug, the volunteers remained on a washout/rest period (it should be a symptom free period between two phases of drug proving in which a volunteer does not take drug) for 14 days and started taking next potency in the same procedure as mentioned above, till completion of 56 doses.

The same procedure was followed for the 3rd & 4th phases.

Each volunteer was interrogated by the Proving Master to verify the sign(s) and/or symptom(s) recorded by the volunteer. The symptoms recorded in 'Prover's Day Book Proforma' were verified by the Proving Master and completed through further interrogation with the provers in respect to their location/ sensation/ modalities and concomitants if any, in 'Symptoms Elaboration Proforma'.

During the course of proving, the volunteers were referred for specific laboratory investigation(s) to rule out any pathological cause of appearance of symptom(s). Since laboratory tests were performed to identify any correlation between the subjective and objective changes during the course of proving, the expert opinion of the honorary consultant(s) was obtained, wherever needed.

After completion of trial of all potencies, the volunteers underwent TME.

On completion of all the phases of the proving, the compilation of data recorded in 'Prover's Day Book Proforma', 'Symptoms Elaboration Proforma', 'Pathological Report Sheets' and 'Terminal Medical Examination sheets', was done at the Council's headquarters by the Drug Proving-cum-Data Processing Cell. After decoding, the sign(s) and/or symptom(s) generated by the volunteers kept on the drug were separated from those generated by the volunteers kept on placebo. The sign(s) and/or symptom(s) which were common to both the groups i.e. placebo as well as drug groups were not taken into consideration while compiling the symptomatology of the drug.

Management of adverse effects:

A vial of antidote is sent with each quota to each center. In this trial homoeopathic potencies of Camphora were used as Antidote as it is believed that Camphora can antidote nearly every vegetable medicine.[10] Proving master gives antidote to the volunteer if symptoms continue for a long time or intensity is much to cause discomfort. Proving Master is also directed to take advice of honorary consultants and to get laboratory investigations done, if required.

Pathogenetic effects

Pathogenetic effects (Proving symptoms) are defined as all changes in clinical events and laboratory findings reported by the volunteers during a Homoeopathic Pathogenetic Trial and recorded in the final report. The incidence of pathogenetic effects per volunteer is defined as the total number of findings observed in the trial divided by the total number of provers.[11]

Pathogenetic effects were deduced

(i) from comparison of symptoms developed in placebo phase with symptoms during intervention phases (Intraprover comparison)

(ii) from comparison of symptoms developed by provers on control (for all phases) with provers on actual drug trial (Interprover comparison)

RESULTS

During the pathogenetic trial, out of 20 volunteers who were in verum group, only 07 volunteers reported symptoms consequent upon the administration of the drug. A total no. of 22 symptoms were produced by the drug so the incidence in this proving was 1.1 findings per volunteer. Any adverse effects were not observed during the trial, so antidote (Camphora) was not used.

The following symptoms were observed during the drug proving:

Information regarding the parenthesis:

- In the first parenthesis, the 1st number given after every symptom denotes number of volunteers who produced that particular symptom and 2nd number denotes potency used.
- In second parenthesis, the 1st number denotes number of doses after which symptom was produced and the 2nd number denotes the duration (in days) for which the symptom lasted.

Head

- Congestive pain in temporal region and thirst with coryza. (1,6C) (20,3)
- Throbbing pain in head with heaviness, more on left side, agg. stooping, moving about, light; amel. cold application , light pressure. (1,30C) (41,2)
- Catarrhal headache. (1,30C) (12,1)
- Pain with heaviness in head and eyes and discomfort in neck agg. bending head forward while reading, light amel. pulling hair, massage, lying down, closing eyes. (1,200C) (44,4)

- Frontal headache, agg. morning, amel. lying down. (1,200C) (28,3)

Eyes

- Burning in eyes. (1,6C) (40,7)
- Pain and heaviness in eye balls extending to back of head and sides of head, amel. sleeping. (1,200C) (20,4)

Throat

- Dryness of throat with pricking pain in left side, as if something is lodged in throat which is not relieved after drinking water, agg. empty swallowing, during sleeping, amel. hot tea and food. (1,30C) (12,3)

Abdomen

- Cramping pain around umbilicus with loose stool, agg. day time. (1,200C) (20,2)

Rectum

- Burning pain in rectum; no relief even after cold application. (1,6C) (44,2)
- Frequent loose stools with pain in right side of abdomen, agg. morning. (1,200C) (40,3)

Stool

- Watery, yellowish-brown, offensive. (1,200C) (20,2)
- Mixed with mucus. (1,200C) (40,4)

Female

- Menses with slight pain, red small clots. (1,6C) (12,5)
- Menses with pain in lower abdomen, back and both legs; flow delayed, profuse, black, clotted. (1,200C) (30,8)

Chest

- Palpitation, feeling of whole body moving with beating of heart in morning after profuse menses. (1,200C) (32,4)

Back

- Tearing pain in nape of neck, radiating towards shoulder, agg. keeping head straight. (1,200C) (42,4)

Extremities

- Red eruptions on thighs and elbows with itching and burning, amel. by scratching. (1,30C) (32,3)

Sleep

- Sleepiness. (1,6C) (44,1)

Fever

- Fever with headache and running nose. (1,30C) (32,3)

Skin

- Itching without eruptions, agg. covering, evening, night, amel. scratching, cold application. (1,30C) (24,3)

Generalities

- Restless, changes position and moves about, agg. at night (1,200C) (44,2)

DISCUSSION

Drug was able to produce symptoms in 6C, 30C and 200C potencies. 22 symptoms were produced by the volunteers in verum group in 2nd, 3rd & 4th phases. 11 symptoms were produced in 200C potency, 6 symptoms were produced in 30C potency and 5 symptoms were produced in 6C potency.

The pathogenesis of the drug was produced in almost all organs and systems of body. During pathogenesis drug produced various types of headache; dryness and pricking pain in throat etc. There was burning sensation in eyes, burning pain in rectum and reddish eruptions with itching and burning. Some other symptoms like cramping pain in umbilicus with loose stool and palpitation were also produced during the study.

These symptoms may help in clinical application of the medicine.

CONCLUSION

The symptoms appeared during the trial will add to the available literature on this medicine and benefit the research scholars and clinicians. These proved symptoms need further verification through clinical application in different clinical settings.

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