Andrographis paniculata - A multicentric, randomized, double-blind homoeopathic pathogenetic trial

Rajpal*[1], Vinay Kr. Singh[1], B.N. Dutta[2], S. Das[2], P.C. Mal[3], A.K. Bhakat[3], R.K. Roy[4], C.P. Chaudhary[4]

[1]Central Council for Research in Homoeopathy, New Delhi, India
[2]Drug Proving Research Unit (H), Kolkata, West Bengal, India
[3]Drug Proving Research Unit (H), Midnapore, West Bengal, India
[4]Drug Proving Research Unit (H), Ghaziabad, Uttar Pradesh, India

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

Methodology: Drug *Andrographis paniculata* was proved by the Central Council for Research in Homoeopathy through double-blind, randomized, placebo-controlled method. The study was conducted at three centers. The drug was proved in two potencies (6C and 30C) on 39 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 two 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 all the three centers was compiled at proving-cum-data processing cell at CCRH headquarters after de-coding.

Observations: Out of the 23 provers who were on actual drug trial, 06 manifested symptoms. Drug was able to produce symptoms in both the potencies more or less related to every part of the body. Some of the symptoms have been reproved which are mentioned in different literatures after the fragmentary proving.

Conclusion: New and reproved pathogenetic responses elicited during the proving trial expands the scope of use of the drug *Andrographis paniculata* 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; *Andrographis paniculata*

INTRODUCTION

The shrub is well known as “Kalmegh” and forms the principle ingredient of household medicine called ‘Alui’ which is extensively used in Bengal. The macerated leaves and juice together with certain spices are made into little globules, which are prescribed for infants to relieve griping, irregular stools and loss of appetite. The roots and leaves have also the reputation of being a febrifuge, tonic, alterative and anthelmintic. In general debility, dysentery and certain forms of dyspepsia associated with gaseous distension of the bowels, the decoction or infusion of the leaves have been used with satisfactory results.[1,2] Brigade Surgeon G.G. Hunter considered this superior to quinine. Green leaves are given with aniseed (4 to 20 in numbers) as

* *Address for Correspondence:*
Dr. Rajpal, Asstt. Director (H)
Central Council for Research in Homoeopathy
61-65, Institutional Area, Janakpuri,
New Delhi- 110 058
Email: ccrhdp@yahoo.com

a stomachic and anthelmintic. Green leaves with the leaves of *Aristolochia indica* and fresh inner root bark of country *Sarsaparilla*, made into an electuary, is used by Hakims of India as a tonic and alterative in syphilitic cachexia and foul syphilitic ulcers.[3] *A. paniculata* may be a safe and efficacious treatment for the relief of symptoms of uncomplicated upper respiratory tract infection.[4]

Dr. Pramada Prasanna Biswas of Pabna, Bangladesh and Dr. N. Sinha made provings of this drug.[2] As both the provings were incomplete and fragmentary, a systematic Homoeopathic Pathogenetic Trial (HPT) of *Andrographis paniculata* 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	:	*Andrographis paniculata* Wall. ex Nees[5]
Family	:	Acanthaceae[3]
Common names[2]	:	
Sanskrit	:	*Kirata,Bhunimba, Mahateekta*
Hindi	:	*Kiryat*
Bengali	:	*Kalmegh*
Marathi	:	*Olenkirayet*
Telugu	:	*Nalavemu*
Tamil	:	*Nilavambu*
Kannad	:	*Nelaberu*
Malayalam	:	*Nelavoepu*
English	:	*The Creat, King of bitters*

Description

An erect annual shrub, 30-90 cm high, branches sharply 4 angled or almost winged. Leaves 5.8 cm long, lanceolate, acute, tapering at the base, pale beneath, main lateral nerves 4-6 pairs, petioles none or upto 0.6 mm long. Flowers small solitary,arranged in lax spreading axillary and terminal racemes or panicles, the pedicles distinct gland-pubescent; bracts 2.5 mm long lanceolate, bracteoles smaller or none. Calyx 3 mm. long, segments equal, linear-lanceolate; Corolla pink, 1cm. long hairy outside, tube 5mm long, dilated below the limb. Filaments hairy upwards, rugose, glabrous.[6]

Distribution

This annual is common in hedgerows throughout the plains of India, cultivated in gardens from Lucknow to Assam, especially in Bengal. [3]

Part used in Homoeopathy

Whole plant.[6]

Potencies used

6C & 30C

MATERIALS AND METHODS

Objective

To elicit the pathogenetic response of the drug *Andrographis paniculata* on apparently healthy human volunteers in homoeopathic potencies. The latent healing power of a drug is unfolded by the method of 'Potentization' i.e. successive dilution followed by agitation and this is exhibited in the form of various signs and symptoms produced by the drug when it is given to healthy human beings.

Study Design

The study was a randomized double blind placebo controlled trial.

Participants

Total 39 apparently healthy volunteers from three centers, between the age group of 18 to 50 years, comprising of 26 males and 13 females, were enrolled in this study. All volunteers were screened strictly by the experts. Pre-trial Medical Examination (PME) 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.

Settings & locations

The proving was conducted at Drug Proving Research Units (Homoeopathy) at Kolkata, Midnapore and Ghaziabad from 2005-2006.

Intervention

In the first phase volunteers were given 56 doses (04 doses per day for 14 days) of placebo. In the next two phases 56 doses (04 doses per day for 14 days) of each potency or placebo were consumed according to the randomization.

Drug

Andrographis paniculata was procured in 6C and

30C 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.

Outcomes

The volunteers were asked to stop taking the drug/ placebo as soon as they felt any change or any sign(s) and/or symptoms(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.

To enhance the quality of observations, each prover was interrogated everyday by Proving Master about the appearance of new symptoms or progress of symptoms and noted those in 'Symptom Elaboration Proforma' with respect to appearance and disappearance of symptoms, their location, sensation/ character, modalities, concomitants, extension of symptoms, causation, clinico-pathological findings and other treatment taken.

Randomization

Implementation: Allocation and assignment were done at the headquarters. Enrollment was done at the Drug Proving unit level.

Blinding (masking): The provers and proving masters at the centers were kept blind, as the randomization was done at the headquarters by the co-coordinator of the Drug Proving programme.

Methods

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.

'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 three centers. Out of total 39 volunteers, 23 were kept on drug (verum) and 16 were on placebo (control) in all three phases. All the volunteers were assigned code numbers and the coded drugs of different potencies (including placebo) 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).

The study consisted of three 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.

Procedure of Proving

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

The volunteers 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 they felt any change or developed any symptoms(s) and/or sign(s).

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 symptoms(s) and/or sign(s) appeared with date, time of onset and duration for which they persisted. Intake of drug remained suspended till the symptoms(s) and/or sign(s) or 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 symptoms(s) and/or sign(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 and other treatment taken.

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

If no symptom was observed, 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 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 phase.

Each volunteer was interrogated by the Proving Master to verify the symptom(s) and/or sign(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 Terminal Medical Examination (TME).

On completion of all the respective 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 well known that *Camphora* can antidote nearly every vegetable medicine.[7] 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.[8] So, incidence in this proving was 1.34 findings per volunteer.

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 23 volunteers, only 6 volunteers reported symptoms consequent upon the administration of the drug.

The following symptoms were observed during the drug proving:

- In the first parenthesis, the 1st number given after every symptom denotes number of volunteers produced that particular symptom and 2nd number denotes potency used.
- In second parenthesis, the 1st number denotes number of doses after which symptom produced that particular symptom and the 2nd number denotes the duration (in days) for which the symptom lasted.
- Symptoms produced during the pathogenetic trial of the drug were compared with the homoeopathic literature cited in the reference and those symptoms which were found in the literature, are shown in **bold**, superscribed with a numerical that refers to the respective literature.

Head

- Rolling of head towards left with drowsiness, weakness and nausea in forenoon. (1, 6C) (39,2)
- Pricking pain in right side of head at 7 pm, *agg.* touch, combing. (1, 30C) (3,1)
- Sudden, violent headache with dimness of vision, rolling of head, nausea and feeling of **heaviness of head**[2]; more on right side and gradually extending over the whole head. *agg.* movement and noise, *amel.* tight bandage, warm application and lying quietly. (1, 30C) (34,1)
- Throbbing pain in forehead at midnight, *amel.* pressure. (1, 6C) (31,1)
- Intense itching in occipital region without eruption in afternoon, *amel.* applying cold water. (1, 6C) (39,1)

Eyes

- Twitching of right eyelid. (1, 30C) (56,8)

Nose

- Coryza, **sneezing**[2,9] with **watery discharge**[2,9] and stoppage of nose in morning. (1, 30C) (37,3)
- Coryza with watery discharge; headache and bodyache. (1, 30C) (44,3)
- Burning sensation in nose with watery discharge. (1, 30C) (52,1)
- Dryness of nose with sneezing and dry cough, *agg.* after eating, evening. (1, 6C) (40,9)
- Stoppage of right nostril, crusts, pain in right side of forehead *amel.* steam inhalation. (1, 6C) (49,9)

Mouth

- Painful, whitish, solitary, ulcer with depressed round borders on right edge of tongue with burning pain, a*gg.* spicy food, cold drinks, talking, touch, at night, *amel.* warm drinks. (1, 6C) (33,8)

Ext. Throat

- Hard, painful, tender inflammation of left cervical lymph nodes causing difficulty in deglutition of solid food and drinking. It is associated with dry cough, *agg.* in cold open air, night, *amel.* warm drinks. After some days pain appeared in right side of neck with little swelling of cervical lymph nodes with relief in pain and swelling of left sided cervical lymph nodes. (1, 6C) (39,17)

Stomach

- Appetite decreasing esp. at night. (1, 6C) (24,3)
- Nausea, vomiting of little quantity of watery fluid with loss of appetite. (1, 6C) (39,3)

Abdomen

- Pain in abdomen, *amel.* pressure. (1, 6C) (24,1)
- Pain in left side of abdomen with backache, *amel.* pressure. (1, 6C) (27,1)

Rectum

- Sudden urge for stool, 3-4 times. (1, 30C) (30,5)
- Severe pain in rectum during **loose**[2,9], mucoid stool. (1, 30C) (33,1)
- Severe pain in rectum before and during loose stool with blood stained mucus, *amel.* after stool. (1, 30C) (33,2)
- Severe pain in rectum before and during loose stool, *amel.* after stool. (1, 6C) (28,2)
- Burning pain in anus before and after sticky, soft

stool with difficulty to evacuate and wash from the pan. (1, 6C) (24,6)

- **Frequent**[2,9], watery, loose stool with no smell associated with fever, thirst, restlessness, sweat and anorexia. (1, 30C) (51,5)

Female

- Menstrual bleeding bright red, clotted. (1, 30C) (24,2)

Cough

- Dry cough with pain in chest *agg.* morning with fever, loose stool. (1, 30C) (51,5)

Extremities

- Aching pain in right shoulder and left wrist joint, *agg.* motion, touch, night, *amel.* warm application, resting of part. (1,6C) (45,9)

Skin

- Eruptive rash on chest with itching and burning pain, *amel.* bathing; followed by fever. (1, 30C) (8,1)

Fever

- Fever started at 11 pm and remained whole night. (1, 30C) (24,1)

- Watery nasal discharge, sneezing, burning in eyes with fever (102^0F-103^0F), frontal headache, pain in jaw, hoarseness of voice, loss of appetite, sleeplessness and weakness. Pain in legs, back with fever *amel.* pressure. (1,6C) (28,2)

- Fever (100^0 F) **with chilliness**[2,9], sweat, **headache**[2,9], bodyache, restlessness, weakness, anorexia, excessive **thirst**[2,9] and desire to urinate in morning with nausea and loose stool *amel.* warm drinks. (1, 30C) (51,5)

Generalities

- Lethargy and weakness. (1, 6C) (39,3)

Discussion

Out of the 23 provers who were on actual drug trial, 06 manifested symptoms. Drug was able to produce symptoms in 6C and 30C potencies. Out of 31 symptoms produced by the volunteers on verum group in 2nd or 3rd phases, eight symptoms which are already in the available literature were reproved.

The pathogenesis of the drug was produced mainly nasal, gastro-intestinal and fever symptoms. During pathogenesis drug also produced various types of headache. In a prover the drug showed its peculiar affinity on cervical lymph nodes, in whom left sided cervical lymph nodes were inflamed at first and then right sided cervical lymph nodes also got affected later. The drug also showed affection on joints in its pathogenesis. During the trial drug produced fever with chilliness, sweat, thirst, headache, restlessness and weakness.

New and reproved pathogenetic responses elicited during the proving trial expands the scope of use of the drug *Andrographis paniculata* and will benefit the research scholars and clinicians. The proving symptoms will carry more value when verified clinically.

Acknowledgements

The authors are grateful to Dr. Alok Kumar, Director General In-charge, CCRH for his persistent encouragement and enthusiastic support for the preparation of the article. We also acknowledge Prof. C. Nayak, former Director General, CCRH headquarters, for providing valuable guidelines for conducting and supervising the study.

References

1. Chopra R.N. Indigenous Drugs of India, Academic Publishers, Kolkata, 2nd Edition 2006: 278.
2. Ghosh S.C. Drugs of Hindoostan. 9th Edition. M/s Hahnemann Publishing Co. Pvt. Ltd., Kolkata, 2007: 62-68.
3. Nadkarni K.M. Indian Materia Medica. Bombay Popular Prakashan Pvt. Ltd., 1976, 101-103.
4. Coon JT, Ernst E, Andrographis Paniculata in the treatment of upper Respiratory Tract infections: a systematic review of safety and efficacy. Planta Med. 2004; 70 (4): 293-8.
5. Anonymous. The Useful Plants of India, Publications and Information Directorate, Council of Scientific and Industrial Research, New Delhi, 1986: 39.
6. Anonymous. Andrographis paniculata. Homoeopathic Pharmacopoeia of India, Vol. 1, The Controller of Publications, Govt. of India, Ministry of Health and Family Welfare, New Delhi,1971:54.
7. Allen H.C. Allen's Key Notes and Characteristics with comparisons of the leading remedies of the Materia Medica with Nosodes, 8th Edition, M/s B. Jain Publishing (P) Ltd., New Delhi, 1997: 78.
8. F. Dantas, P.Fisher, H.Walach et. al. A systematic review of the quality of homeopathic pathogenetic trials published from 1945 to 1995. *Homeopathy*. 96 (1), 2007 Jan: 4-16
9. Boericke W. New Manual of Homoeopathic Materia Medica with Repertory. 9th Edition. M/s B. Jain Publishers (P) Ltd., New Delhi, 2007: 974.