

Significance of Prognostic Factor Research in clinical verification

HISTORICAL BACKGROUND: VERIFICATIONS AS NON-PLUS ULTRA!

The verification of drug-proving symptoms has been an essential aspect in clinical practice since Hahnemann discovered Homoeopathy. 'Here a drug is given to the sick, according to the symptoms, it had produced on the healthy (provings) human being and the cures made were the verifications'.^[1] Only by clinical verification, a proving symptom will prove its validity as homoeopathic symptom and cement its value for the practicing physicians. Hahnemann was well aware of the need of clinical verification of proving symptoms when he wrote in his letter to Boenninghausen dated 16th March 1831: 'There are indeed still many obscure and only partially correct items in the current list of symptoms which are in desperate need of verification.... We need thousands of drug provers and a well-equipped hospital..... clinical verification is mandatory, without which the "Pure Materia Medica" cannot be ascertained'.^[2] Boenninghausen also concurred with Hahnemann, about the need to verify the action of drugs and clarified the process in the preface of Boenninghausen's Therapeutic Pocket Book. He emphasised on repeated and adequate verifications of the action of a drug before its entry into repertory as a remedy with high grade. Dr. Hering, further streamlined this process when he stated that a symptom does not acquire the status of a guiding symptom unless, apart from its appearance in the provings, it has been verified at the bedside a number of times.^[3] Thus, grading of remedies in the first-line Materia Medica and repertories of homoeopathic stalwarts were based on how frequently a particular symptom was verified, and verifications were the non-plus ultra of those times.

VERIFICATIONS AS MISSING LINK!

The importance of clinical verification of proving symptoms is historical and even more importantly, relevant to validate 'modern' homoeopathic practice. It is the study of the link between pathogenetic symptoms and curing of patients presenting these symptoms. An unconfirmed proving symptom that never was verified by clinical data cannot yet be considered as useful for homoeopathic practice.^[4] Verification of homoeopathic symptoms has so far been a neglected field. Over the time, the clinical symptoms, whether or not verified, have found a place in textbooks. Based on expert opinion, entries in homoeopathic repertory are done. The most serious flaw of such repertory is that majority of entries are based on absolute occurrence of symptom in the cured or partially improved population and have no relation with its prevalence

in general population. Ideally, a symptom, thus, is an indication for a specific medicine only if the prevalence of that symptom is higher in the population cured by that medicine than in the rest population^[5] such verifications shall give more reliability and helps us in creating an authentic Materia Medica.

CLINICAL VERIFICATION PROGRAMME OF CENTRAL COUNCIL FOR RESEARCH IN HOMOEOPATHY: A NICHE AREA OF FIELD DATA

Council has been conducting clinical verification studies of indigenous, rare and fragmentarily proved drugs since its inception in 1978. The primary objective of the study was to clinically verify the symptomatology of the drug as observed during proving or as mentioned in other literature. The secondary objective was to ascertain the clinical symptoms that did not appear during the proving but were improved in the patients after its administration, either completely or partially. The medicines were prescribed based on symptom similarity. The individualistic symptoms of each case are evaluated as per the Materia Medica and repertorial index especially devised for the programme from the proving data. Clinical verification of symptomatic data of 106 drugs has been conducted so far in real-time practice. Thousands of proving symptoms have been verified in over 20,000 study subjects in this programme. The data thus obtained have been disseminated in the form of 3 books, 19 monographs and 62 articles of which 18 are in peer-reviewed journals. Council improvised its protocol in 2013 by including scales to assess patient and remedy reactions. The notable inclusion was the modified Naranjo criteria for assessing the causal attribution of change (i.e. attribution of observed changes to a particular remedy) after prescriptions in conformation with international standards.^[6-8] Central Council for Research in Homoeopathy has been following traditional method of verification since inception where the symptoms verified depended on the number of subjects improved/not improved alone and not subjected to any further analysis. This has been modified and elements of prognostic factor research have been included but analysing the existing data where information about the prevalence of symptoms in general population was not recorded remains a challenging task. In a series of papers,^[9-11] the data of verification of four lesser-known homoeopathic medicines (*Cynodon*, *Formic acid*, *Ocimum canum* and *Mangifera indica*) were published with an impressive number of cases. Retrospective assessment of prevalence and likelihood ratio (LR) of symptoms in good responders could be a mean for better selection of symptoms for prospective research, but feasibility of conducting

such retrospective analyses was a fine point of contention. Finding out the prevalence of these symptoms in remainder of the general population treated during the study was not feasible since it was outside the scope of the protocol. Hence, formulation of 2×2 contingency table for calculation of LR did not seem possible at that point of time. Therefore, all the results deduced in these experimental articles should be considered as provisory and need further confirmation through prospective research in a larger sample size.^[12-14]

In these articles, we compared responding and not-responding patients for one medicine. Only some ideas of symptoms that can be further investigated were derived. The symptom prevalence should necessarily be higher in the responding population than in the whole population – ‘not just the not-responding population’-to be considered as an indication for the given medicine. The prevalence of any symptom under investigation can probably be best assessed in multi-centre clinical verification programmes that could produce more reliable and generalisable nation-wide data.^[11] We must realise that such a research has a greater sensitivity for confirmation bias. Biased data, however, will have a negative influence on the reliability of our Materia Medica and repertoires.^[15,16]

Council has so far experimented with small and lesser known remedies following a specific policy^[17] to promote focused research on plants of indigenous origin. We have huge data of such experiments, and it is essential to analyse these data appropriately to derive meaningful conclusions for future research. In this issue we are publishing another lesser known drug *Aranea Diadema*, after much review, the analysis cohort of 172 patients is being published. The strength of this research is that it compared the prevalence of symptoms between different medicines.^[18] In the retrospective analysis, only ‘confined LR’ values (confined to the symptoms of group of medicines included in the verification) can only be calculated. The real LR values cannot be calculated as the denominator (prevalence in all the remainder of the population) is not possible to be calculated. The medicines with ‘confined LR’ values >1 , i.e., prevalence above average, could be considered as tentatively confirmed, but these LR values cannot yet not be used for entries in respective repertory rubrics.

In addition, we are publishing a single-blind, randomised, placebo-controlled pilot study to evaluate Homoeopathy in polycystic ovarian syndrome; some positive results were observed which are shared with readers in this issue. In spite of some limitations in the form of the short duration of follow-up, non-blinding, the primary objective, i.e. the establishment of the regular menstrual cycle along with improvement in either ultrasonology or hirsutism/acne was achieved in 60% cases in the arm with Homoeopathy along with lifestyle modifications.^[19] The role of Homoeopathy in dental ailments is assessed in an article in this issue. In this study on 80 patients, *Belladonna* was compared with *Ibuprofen* in control of orthodontic pain during orthodontic separation. There was no statistically significant difference between *Belladonna* and

Ibuprofen groups; lack of adverse effects in *Belladonna* can be considered as better and viable option for patients undergoing dental procedures^[20] having known sensitivity to ibuprofen or with chronic renal diseases.

So far, many impressive results have been obtained from *in vitro* studies done on Homoeopathic preparations. In this issue, *Cephalandra Indica* potencies were assessed for its phenolic content, antioxidant capacity, reducing power and radical scavenging activities to exhibit its protective effect against oxidative stress.^[21] Role of animal model experiments in Homoeopathy has been previously discussed.^[22]

Further, pharmacognostic and physicochemical study of *Polygala Senega* has been conducted by author as pharmacopoeial standards for identification and authentication of this homoeopathic drug.^[23] Adding to research evidence, case reports on breast fibroadenoma.^[24] Furthermore, a book on the research of Homoeopathy in Gynaecology has been analysed under book review section.^[25] The author has demonstrated that by meticulous record management even in private clinic can create a valuable manuscript for the profession.

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REFERENCES

- Hering C. The Guiding Symptoms of our Materia Medica. Reprint edition. Vol. 1. New Delhi: B. Jain Publishers (P) Ltd.; 2000. p. 6-7.
- Wassenhoven MV. Clinical Verification – Verification of Homeopathic Symptoms. New Delhi: B. Jain Publishers; 2008.
- Available from: <http://www.wholehealthnow.com/bios/constantine-hering.html>. [Last accessed on 2018 Mar 22].
- Available from: http://www.wisshom.de/dokumente/upload/ae78e_e2dd4_2013_guidelines_clinical_verif_hom_symptoms_third_edition.pdf. [Last accessed on 2017 Nov 20].
- Rutten L, van Wassenhoven M. Clinical verification of homeopathic symptoms: Experience and statistics. In: Bonamin LV, editors. Signals and Images. Dordrecht: Springer; 2008.
- van Haselen RA. Homeopathic clinical case reports: Development of a supplement (HOM-CASE) to the CARE clinical case reporting guideline. Complement Ther Med 2016;25:78-85.
- Riley DS, Barber MS, Kienle GS, Aronson JK, von Schoen-Angerer T, Tugwell P, et al. CARE guidelines for case reports: Explanation and elaboration document. J Clin Epidemiol 2017;89:218-35.
- Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 1981;30:239-45.
- Manchanda R, Chakraborty P, Das KC, Rai MK, Singh O, Pradhan PK, et al. Symptom prevalence in a cohort of 147 patients improved with the homoeopathic medicine *Ocimum canum*: A multicenter, open, observational, clinical verification study. Indian J Res Homoeopathy 2016;10:238-48.
- Manchanda R, Chakraborty P, Singh P, Pradhan PK, Prasad VG, Singh O, et al. A multicenter, observational, homoeopathic clinical verification study of *Cynodon dactylon* revealing symptom prevalence in a cohort of 340 patients. Indian J Res Homoeopathy 2016;10:225-37.
- Manchanda RK, Chakraborty PS, Singh P, Rai MK, Singh O, Singh DK, et al. Symptom prevalence in a cohort of 65 patients improved with the homoeopathic medicine *Mangifera indica*: A multicentric open observational clinical verification study. Indian J Res Homoeopathy 2017;11:184-95.
- Rutten L, Manchanda RK. Homoeopathy: Discussion on scientific

- validation. *Indian J Res Homoeopathy* 2016;1:66-74.
13. Rutten L. Data collection: Treat every variable as a treasure. *Homoeopathy* 2015;104:190-6.
 14. Eizayaga JE, Pozzi MI, Canan MC, Saravia L. Prevalence and likelihood ratio of symptoms in patients with good therapeutic response to *Lycopodium clavatum*. A retrospective study. *Homeopathy* 2016;105:78-83.
 15. Available from: <http://www.lmhi.org/downloads/nvp/LMHI%20Sc%20framework%202016-modi.pdf>. [Last accessed on 2017 Dec 26].
 16. Rutten L, Muraleedharan KC, Shinde VH, Manchanda RK. What is a homoeopathic symptom, in daily practice and research? *Indian J Res Homoeopathy* 2017;11:12-20.
 17. Available from: http://www.ayush.gov.in/sites/default/files/7870046089-Ayush%20n%20policy%20ISM%20and%20H%20Homoeopathy_0.pdf. [Last accessed on 2017 Dec 24].
 18. Gupta J, Manchanda RK, Chakraborty P, Singh P, Ramteke S, Singh O, *et al.* Prevalence and prognostic factor in patients with good therapeutic response in a cohort of 172 patients with the homoeopathic medicine *Aranea diadema*: A multi centre, open-label, observational study. *Indian J Res Homoeopathy* 2018;12:20-26.
 19. Lamba CD, Oberai P, Manchanda RK, Rath P, Bindu PH, Padmanabhan M. Evaluation of homoeopathic treatment in polycystic ovary syndrome: A single-blind, randomised, placebo-controlled pilot study. *Indian J Res Homoeopathy* 2018;12:35-42.
 20. Patil HA, Patil J, Kerudi VV, Hamid T, Jaltare P, Sharan JS, *et al.* Comparison of efficacy of ibuprofen and *Belladonna* in the control of orthodontic separator pain. *Indian J Res Homoeopathy* 2018;12:29-34
 21. Kishore L, Singh R. Effect of *Cephalandra indica* against AGEs, sorbitol accumulation and aldose reductase activity in Homoeopathic Formulation. *Indian J Res Homoeopathy* 2018;12:11-19.
 22. Manchanda RK. Significance of animal model research in homoeopathy. *Indian J Res Homoeopathy* 2017;11:1-4. Available from: <http://www.ijrh.org/text.asp?2017/11/1/1/200846>. [Last accessed on 2018 Mar 19].
 23. Patel S, Biswas B, Nagaraju M, Jhansi S, Arya R, Sundaram EN. Pharmacognostic studies of *Polygala senega* L. Root- a homoeopathic drug. *Indian J Res Homoeopathy* 2018;12:10.
 24. Parveen S. Individualized homoeopathic treatment of breast fibroadenoma: A case report. *Indian J Res Homoeopathy* 2018;12:46-52.
 25. Gupta G. Evidence-Based Research of Homoeopathy in Gynaecology. Aligarh Lucknow: Gaurang Clinic and Centre for Homoeopathic Research; 2017.

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Access this article online	
Quick Response Code: 	Website: www.ijrh.org
	DOI: 10.4103/ijrh.ijrh_21_18

How to cite this article: Manchanda RK. Significance of prognostic factor research in clinical verification. *Indian J Res Homoeopathy* 2018;12:1-3.