Homeopathy (2013) 102, 207–214

http://dx.doi.org/10.1016/j.homp.2013.02.002, available online at http://www.sciencedirect.com

ORIGINAL PAPER

Hepatitis C Nosode: The preparation and homeopathic pathogenetic trial

Rajesh Shah*

Life Force, 411 Krushal commercial Complex, G.M.Road, Chembur, Mumbai 400 089, India

Background: **A double blind, randomized placebo controlled homeopathic pathogenetic trial (proving) of Hepatitis C (Hep C) nosode was conducted with the aim to introduce the new nosode in homeopathic pharmacopeia.**
Method: **Documentation included approval by Ethics Committee, Informed Consent Form, Laboratory investigations, safety and ethical measures. The volunteers were trained to write data in prescribed diaries and data were analyzed. A fifteen-step method was used in the preparation of Hep C nosode (genotype I and III), allowing future preparation of an identical nosode. 22 volunteers were entered, 15 received Hep C nosode in 30c potency, 7 received placebo, once a week for four weeks.**
Results: **The Hep C nosode was associated with qualitatively and quantitatively distinct symptoms, which can be applied in clinical practice. A significantly higher incidence of pathogenetic effect of homeopathic medicine compared to placebo was observed. Safety was documented. The nosode produced symptoms comparable with Hep C disease.**
Conclusion: **An improved method of nosode preparation was used. A double blind, randomized placebo controlled pathogenetic trial of the Hep C nosode generated guiding symptoms, which may facilitate its prescription in practice. The nosode should be further explored for the treatment of immunologically mediated diseases, infections including Hep C, fibrotic pathology and chronic inflammatory disorders.** *Homeopathy* (2013) **102**, 207–214.

Keywords: Hepatitis C; Nosode; Drug proving; Homeopathic pathogenetic trial; Potentization; Standardization; Double blind; Randomization; Placebo control; Safety; Symptoms

Introduction

The Hepatitis C virus, previously known as non-A, non-B virus, was postulated in 1970 and demonstrated in 1989.[1] Hepatitis C is a serious and chronic infection. An estimated 130–170 million people worldwide and about 1.4% Americans are infected with hepatitis C.[2,3] The epidemiology of hepatitis C in India has not been studied systematically.[4] Hepatitis C causes hepatitis, cirrhosis, malignancy, fibrotic changes, thrombocytopenia, hepatic portal hypertension, chronic organ inflammation, etc. Hepatitis C is the cause of 27% of cirrhosis cases and 25% of hepatocellular carcinoma worldwide.[5]

The method of nosode preparation used for the product test in this trial was designed and approved with the help of a team comprising virologist, immunologist, biotechnologist, legal attorney, homeopaths, pharmacologist, microbiologist, social worker, and hepatologist.

In this project, placebo effects were filtered out by:

1. Placebo controlled, blinded, randomized design.
2. Elimination of study of symptoms if they also occurred in run-in period, in the same volunteer.
3. Comparison of proving symptoms with known symptoms of the disease.
4. Quantification of duration and intensity of symptoms and days of appearance, quantified.

*Correspondence: Life Force, 411 Krushal commercial Complex, G.M.Road, Chembur, Mumbai 400 089. India.
E-mail: sanjivak@gmail.com
Received 7 June 2012; revised 22 January 2013; accepted 5 February 2013

5. Number of volunteers who produced particular symptoms.

The study has substantiated previous work.[6,7] The project of Homeopathic pathogenetic trial (drug proving) was designed to evaluate the clinical symptoms of Heptatis C (Hep C) nosode in healthy volunteers. Volunteers were blind to the identity of the substance as well as to whether they received verum or placebo.

Objective

To prepare a polyvalent Hep C nosode using a well-defined, standardized method. To conduct a double blind placebo controlled pathogenetic trial with the Hep C nosode, on healthy humans with the aim of deriving indications for clinical application.

Materials and methods

Preparation of nosode

The Hep C nosode was prepared using an elaborate 15-step method (patent pending with the author); as the method underwent some technical modernization. In brief, Institutional Ethics Committee approved the project of Hep C nosode preparation. Informed consent forms were served to the patient-volunteers who donated their blood. Two patients were separately screened with Hep C geno-type I and III respectively, were ruled out for possible co-infections such as HIV, Hep B, Gonorrhea, Syphilis, etc.; blood was drawn, serum expression was done, serum filtration was carried out to remove large particles and other possible bacteria.

This resulted in serum containing specific number of Hep C virus particles, without other possible co-infections as well as large protein particles. The serum was standardized in terms of viral load using the RT-PCR method. Hep C genotype I virus copies were 2,94,000 IU/ml and Hep C geno-type III virus copies were 10,30,000 IU/ml. Some amount of sera was lyophilized for future use. 0.03 ml each of Hep C geno-type I and III were mixed with 2.94 ml of water for injection (as vehicle) for potentization.

To further standardize the potentization process, force parameters of the mechanical potentizer were documented. Potencies up to 15c were prepared using water for injection and subsequently (up to 30c and more) with alcohol as vehicle, with 0.03 ml−2.97 ml (1:99) ratio. Micropipettes were used instead of following *drop* method. Safety check (for human use) was carried out for Hep C nosode 30c potency by RT-PCR method. Samples of HCV nosode 30c potency were tested for presence of HCV virus by Hepatitis C virus (HCV) RNA quantification (viral load), COBAS TaqMan method, which was done with multiple samples, by spiking with positive and negative controls. The serum of mother preparation (containing Hep C virus) was used as positive control. It was established and documented that all the samples of HCV nosode 30c were negative for HCV virus. All the blood work was done at accredited Metropolis Laboratory and Reliance Life Sciences Laboratory.

Volunteers and method

The author was the principal investigator; a double blind, randomized placebo controlled study was conducted at Life Force research center. A blinded person who was not involved in the study procedure generated randomization number table. The drug was proved in 30c potency on 22 volunteers with randomization ratio of 2:1, 15 volunteers received and verum, seven volunteers matching placebo. The study involved seven females and 15 males out of 22 volunteers; six females received active and one placebo; nine males received active and six placebo.

The dose and repetition was 30c potency, one dose, once a week for 4 weeks. Volunteers and investigator were blinded to the identity of the substance and verum/placebo allocation. The volunteers signed Informed Consent Forms. Blinding was maintained until the completion of the proving period. The proving volunteers were selected based on the inclusion and exclusion criteria. The volunteers, aged 18−45 years, from different walks of life, including homeopathic students and homeopaths participated. The volunteers underwent the pre-observation and post observation investigations namely X-ray chest, electrocardiogram, routine laboratory investigations and pregnancy tests, as applicable.

Each volunteer completed intake of the five doses, one dose of placebo on the first day with seven days of run-in period; then one weekly dose of medicine for next 4 weeks. The symptoms generated during the trial period were noted (up to 6 weeks) by the volunteers in the diary provided to them and were cross-examined and elaborated by the proving master. Proving master (investigator) had compiled the data after decoding (opening the blind).

Guidelines, ethics, compliance and approvals

We based the pathogenetic trial project on the guidelines advocated by Samuel Hahnemann, MD, in Organon of Medicine, aphorisms 110−145,[8] CCRH (Central Council for Research in Homoeopathy, Government of India)[9] and ECH (European Committee for Homeopathy) guidelines.[10] The project was reviewed and approved on 16th September 2011, by Institutional Ethics Committee (Homeopathy India Pvt Ltd, Mumbai), constituted as per ICMR (Indian Council of Medical Research)[11] guidelines. The requirements regarding the obligations of investigators as per 'Guidance on Good Clinical Practice' as per ICH (International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use Independent Ethics Committee) were complied with. The project was registered (Number: CTRI/2011/12/002314) with the Clinical Trials Registry − India (CTRI),[12] set up by the ICMR's National Institute of Medical Statistics (NIMS).

Investigations

Pre and post-drug-administration investigations included complete blood count, ESR (Erythrocyte Sedimentation Rate), HIV, Hep C screening (HCV-total antibody to hepatitis c virus), serum by EIS (30 method), blood biochemistry, urine routine analysis, pregnancy test, X-ray chest and electrocardiogram. Female volunteers were negative

for pregnancy test before chest X-ray. Other investigations, if indicated were done at the last visit.

Inclusion, exclusion and withdrawal criteria

Inclusion criteria:

i. The volunteer must be healthy in the sense that he should not show significant psychic or physical symptoms and should not consider himself to be in need of medical treatment. Also the PI or his/her associate should not see a necessity for treatment.
ii. The volunteer must be trustworthy, able and ready to express and describe his experiences during the Proving.
iii. There should be no plans for important life changes like relocating, change of job, marriage, and surgical treatment. The usual habits and conduct of life should be continued.
iv. No planned medical or surgical treatments like dentist, surgery or psychotherapy during the drug proving.
v. 18−45 years.
vi. The volunteer must be in such a mental and legal state so as to able to exercise fully his/her choice and written consent should be obtained.
vii. ECG and Chest X-ray reported within normal limits.

Exclusion criteria:

i. Current medical treatments or homeopathic drugs in the preliminary observation period or during the Proving.
ii. Consumption of prescribed drugs (including homeopathic) in the past four weeks.
iii. On contraceptive pills in the past three months.
iv. Surgical treatment within past two months.
v. Pregnancy or lactation.
vi. Allergic manifestations particularly pertaining to respiratory system and skin.
vii. History of diabetes, hypertension and hypothyroid.
viii. Drug addiction.
ix. HCV positive.

Withdrawal criteria:

i. If a volunteer has to be withdrawn because of a severe adverse the data recorded will be considered for analysis. The volunteers will be marked as 'withdrawal'.
ii. Volunteer lost to follow up.
iii. Withdrawal of consent to continue in drug proving study by volunteer.
iv. Withdrawn volunteers were not replaced.

Training

Volunteeers were trained to note symptoms in the diaries provided to them, as soon as possible. Proving coordinator was trained to study cases, review symptoms and coordinate with the healthy volunteers. Records were maintained in the original handwritten diaries (journals) completed by the volunteers. The data was subsequently entered in Excel spreadsheets. Every volunteer received a dose of placebo on day one. The first week was a run-in period; symptoms experienced during the run-in period were documented carefully. One dose of 30c potency or matching placebo was administered to every volunteer, once her week, for four subsequent weeks, unless there were severe symptoms or Serious Adverse Events (SAEs).

Methodological quality

The Methodological Quality Index (MQI) was developed by Dantas *et al.*, based on key components of methodological quality including internal and external validity.[13] The MQI includes aspects such as *randomization, inclusion and exclusion criteria, blinding and criteria for selection of pathogenetic effects*, with values ranging from 1 to 4 for each component, giving a range from 4 to 16. Scores were divided into four methodological classes, where class I is the worst and class IV is the best, with arbitrary cutoff points (≤6 for Class I; 7−10 for Class II; 11−13 for Class III; >14 for Class IV).

Randomization: Pre-generated Random number table was used to allocate the randomization kits to the volunteers as per the recruitment sequence (Score: 4).

Blinding: Double-blind − participant and investigator is blinded. The blind for randomization was maintained till the completion of the proving period. The blind was opened post trial and verified for the volunteers for drug and placebo (Score: 4).

Inclusion and exclusion criteria: The criteria were clearly defined in the protocol (Score: 4).

Criteria for selection of effects:

1. All symptoms produced during run-in period (first week, with placebo) were excluded.
2. Symptoms produced by the volunteers who were dropped out from study due to adverse events were excluded
3. Symptoms produced by placebo group (N = 7), for 5 weeks and symptoms produced by volunteers on drug (N = 15) were analyzed quantitatively as well as qualitatively. E.g. symptom headache reported by only one volunteer in placebo group but reported by three volunteers who were on drug, was not eliminated.
4. All symptoms were reported quantitatively, day wise, with duration and frequency. E.g. Dull headache with heaviness of head all over the head <1−4 p.m. associated with sleepiness. (Number of volunteers: 1) [9^{+} (day 22 for 2−3 h)].
5. Every symptom described by the volunteers has been graded as + (mild), ++ (moderate), +++ (severe) and ++++ (very severe). This method allowed qualification grading.
6. Volunteer who had exhibited some symptoms prior to the drug proving (as per the history), were eliminated, if the volunteer also exhibited same or similar symptoms as an effect of the medicine.

According to these criteria, this study has a maximum MQI score of 16.

Results

The study involved seven females and 15 males; six females received verum (Hep C nosode) and one placebo

(who withdrew consent after one week); nine males received verum and six placebo. The mean age of volunteers 26.14 years. The flow of volunteers through the study is shown in Figure 1.

Adverse event and withdrawal of volunteers

One subject voluntarily withdrew consent after 4 weeks. There were no reported adverse events related to the intake of the nosode. Adverse events are defined as any untoward medical occurrence in a volunteer administered a proving substance and which does not necessarily have a causal relationship with the action of the substance.[5] No volunteer reported SAE or Serious Adverse Drug Reaction (Serious ADR) during the course of drug proving.

Pathogenetic effects

A full listing of symptoms reported by volunteers during the run-in period and while taking placebo and the treatment is given in the web appendix. All 15 volunteers who received Hep C nosode contributed symptoms or signs. One subject (number CR005) withdrew voluntarily after 28 days, symptoms till 28 days were included in analysis. The overall incidence of pathogenetic effects is calculated as follows: The overall incidence of pathogenetic effects = Number of volunteers who had at least one reported pathogenetic effect (15)/Total number of volunteers taking the medicine and who contributed symptoms or signs (15) = 15/15 = 1.

The total numbers of symptoms reported by the 15 volunteers was 135. The incidence of pathogenetic effects per volunteer is calculated as follows: The incidence of pathogenetic effects per volunteer (verum group) = Total number of findings claimed in the trial (135)/Total number of subjects using the medicine and included in its final pathogenetic description (15) = 135/15 = 9.

Thirty symptoms were reported by seven volunteers who received placebo, thus the total number of subjects using the placebo and included in its final pathogenetic description was 30/7 = 4.28.[13]

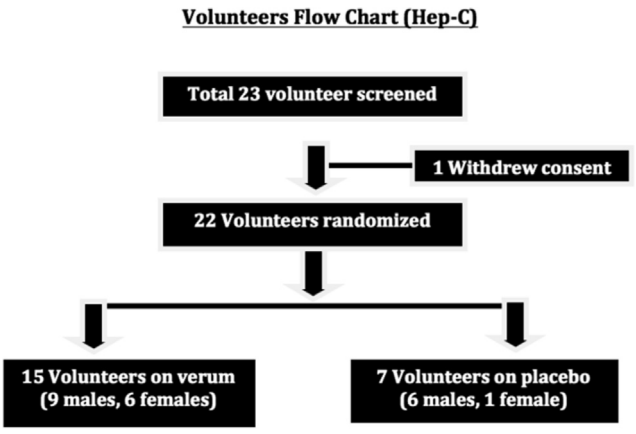

Figure 1 Flow chart of screening, recruitment, randomization and study completion.

Distribution of symptoms

Figure 2 shows the organ distribution of symptoms reported by volunteers, by the country chapter. [Format: Organ$^{(\text{number of volunteers})(\text{volunteer reference number})}$.

Mind$^{(8)(1,5,6,7,9,14,15,16)}$, Dreams$^{(5)(1,2,7,15,18)}$, Head$^{(8)(1,4,5,7,9,13,15,18)}$, Eyes and vision$^{(3)(5,6,14)}$, Nose$^{(5)(2,4,6,9,16)}$, Face$^{(3)(6,7,13)}$, Mouth$^{(3)\ (6,7,13)}$,Teeth$^{(2)(7,14)}$, Throat$^{(4)(1,7,9,13)}$, Stomach$^{(8)(4,15,16,7,13,1,9,22)}$, Abdomen$^{(2)(7,15)}$, Rectum and stool$^{(3)(9,15,16)}$, Male genitals$^{(1)(7)}$, Female genitals$^{(3)(1,4,6)}$, Urinary organs$^{(2)(1,13)}$, Urine$^{(2)(1,13)}$, Chest$^{(1)(1)}$, Cough$^{(3)(4,15,16)}$, Sleep$^{(7)(1,2,4,7,11,\ 13,18)}$, Neck$^{(3)(1,11,15)}$, Back$^{(3)(6,16,22)}$, Extremities$^{(7)(1,4,7,11,15,18,20)}$, Fever$^{(2)(4,14)}$, Skin$^{(6)(1,2,4,5,6,7)}$, Generalities$^{(8)(1,4,6,7,15,16,18,20)}$.

Pathological tests

All the volunteers underwent lab tests, including full blood count, liver function tests, renal function tests, urine analysis and electrocardiograms, before and after the intake of medicines for five weeks (Table 1).

The following abnormalities were detected:

- CR-015 and CR-016: At screening, CR-015 presented with serum glutamic oxaloacetic transaminase (SGOT) 176 and serum glutamic pyruvic transaminase (SGPT) 222; and CR-016 with SGOT 57 and SGPT 102. Being asymptomatic, they were enrolled. Post-drug proving after five weeks, the values for CR-015 were SGOT 56 and SGPT 106, and the values for CR-016 were SGOT 27 and SGPT 56. Since the Hep C nosode has probable influence on liver functions, the altered values have some relevance. This could be either a normal variation or therapeutic action of the nosode. Response in these two volunteers CR-015 and CR-016, calls for further study in a larger sample size.
- CR-016: At screening, the volunteer had Eosinophils 10, and clinically asymptomatic. After 5 doses of the medication, the Eosinophils reduced to 1.
- CR-017: At screening Total Leukocyte Count 5200 value was within normal reference range, which changed to 12,000, post five doses. This volunteer was on placebo.
- CR-022: The TLC 7000 changed to 12,000, after five weeks of medication.
- CR-018: At screening Alkaline phosphatase 132 value was out of normal reference range, in a clinically asymptomatic volunteer, whose value changed to 155 after five doses.

Safety: post-homeopathic pathogenetic trial Hep C infection status

All the volunteers were screened for Hep C infection 6 weeks after starting intake of the medicine, as one of the major concerns expressed by the Ethics Committee was about the risk of Hep C infectivity through homeopathic nosode. No volunteer became Hep C seropositive after the drug proving. Certain changes in liver function tests have been observed and documented (see Table 1).

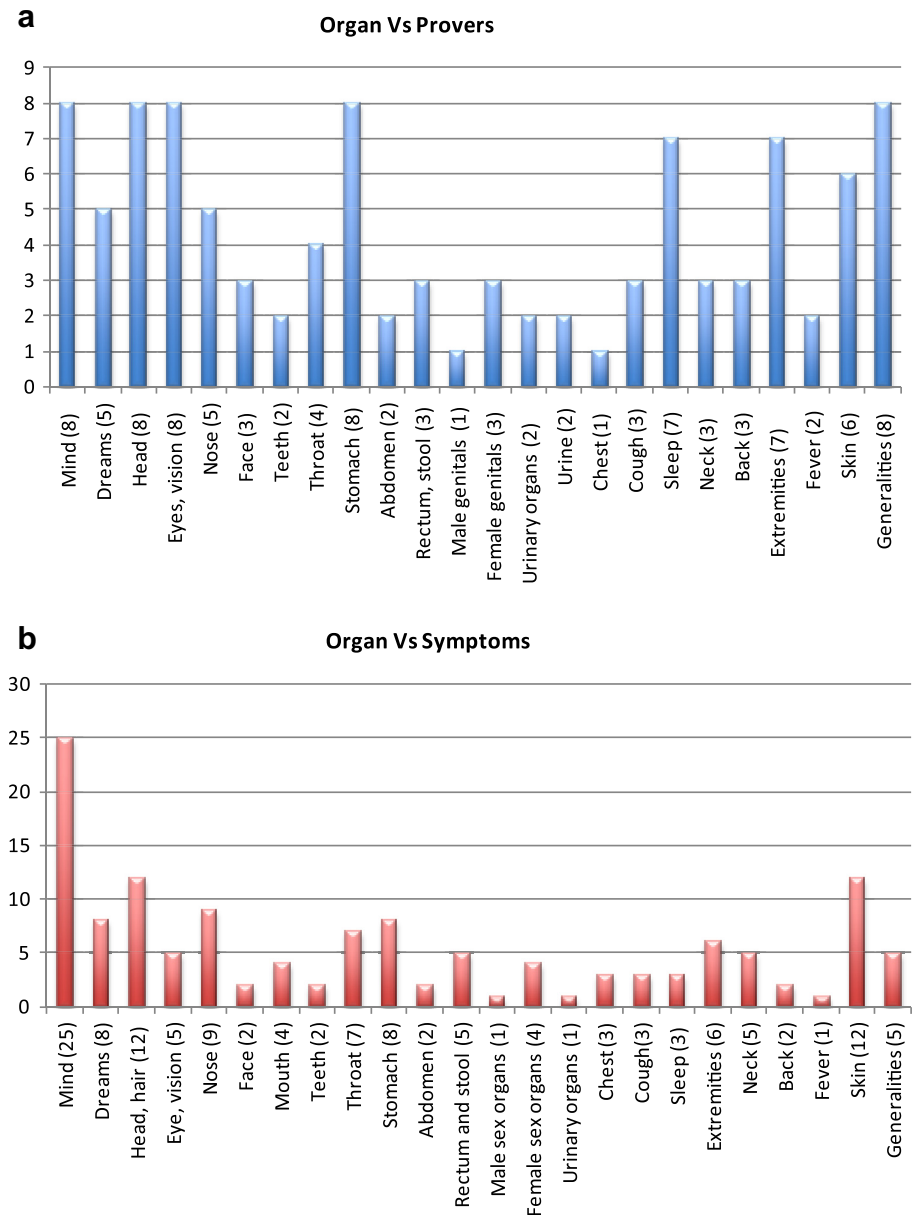

Figure 2 a: Numbers of volunteers reporting symptoms by organ/repertory chapter. b. Number of symptoms per organ/repertory chapter.

Symptoms produced by Hep C nosode

The group which received the Hep C nosode exhibited qualitatively and quantitatively distinct symptoms; the verum group exhibited more symptoms of greater intensity in more volunteers than the placebo group (see Table 2). The incidence of pathogenetic effects per volunteer in verum group versus placebo group, was 9 versus 4.28, 135 symptoms which did not occur in the run-in period, were reported with active treatment. Based on the defined criteria for importance, in terms of intensity and repetition, the following symptoms were retrieved as possibly relevant to clinical practice.

Table 1 Abnormalities in pathological tests before and after the HPT

Sr. no	*Volunteer randomization number*	*Observation*		
		Parameter (normal range)	*Pre*	*Post*
1.	CR-015	SGOT (15–37 U/l)	176	56
		SGPT (30–65 U/l)	222	106
2.	CR-016	SGOT (15–37 U/l)	57	27
3.	CR-016	SGPT (30–65 U/l)	102	56
4.	CR-016	Eosinophils (1–6%)	10.0	1.0
5.	CR-017	TLC (4000–10,500/c.mm)	5200	12,000
6.	CR-018	Alkaline phosphatase (50–136 U/l)	132	155
7.	CR-022	TLC (4000 to 10,500/c mm)	7000	12,000

1. **Mind: Confused feeling** (Number of volunteers: 2) (1^{+++}, 7^{++}). **Dullness of mind** (Number of volunteers: 2) (15^{++}, 16^{++}) **Irritability** (Number of volunteers: 2) (7^{++}, 14^{++}) **Lazy feeling** (Number of volunteers: 2) (6^{+}, 14^{++}) **Weeping** (Number of volunteers: 2) (1^{++}, 5^{++})
2. **Dreams**: **Dreams of snakes** (Number of volunteers: 3) (1^{+++}, 7^{++}, 16^{++})
3. **Head: Head, heaviness of head** (Number of volunteers: 3) (4^{++}, 16^{++}, 18^{+}) **Head, heaviness of head <3 p.m. to 4 p.m.** (Number of volunteers: 2) (13^{++}, 18^{+}) Dandruff. (Number of volunteers: 1) [5^{++} (day 16

Table 2 Numbers of volunteers and symptoms reported in run in and with placebo and verum treatment

No	*Organ*	*Symptoms during run in period with placebo (N = 15)*			*Symptoms with placebo group (N = 7)*			*Symptoms with drug group (n = 15)*		
		No. of symptoms	*No. of volunteers*	*Volunteer's No.*	*No. of symptoms*	*No. of volunteers*	*Volunteer Nos.*	*No. of symptoms*	*No. of volunteers*	*Volunteer Nos.*
1	Mind	3	1	1	2	2	17, 19	25	7	7, 14, 15, 5, 6, 16, 9
2	Dreams	3	2	1, 9	–	–	–	8	5	1, 7, 15, 2.18
3	Head, hair	7	7	2, 9, 6, 20, 16, 15, 11	2	2	17, 19	12	8	7, 1, 4, 15, 18, 13, 5, 9
4	Face	–	–		1	1	8	2	3	7, 6, 13
5	Eyes, vision	3	3	1, 6, 14	–	–	–	5	3	6, 5, 16
6	Nose	1	1	2	1	1	8	9	5	4, 9, 15, 2, 6
7	Mouth	2	2	18, 9	–	–	–	4	3	6, 7, 13
8	Teeth	–	–	–	–	–	–	2		7, 16
9	Throat	3	3	8, 9, 16	2	1	8	7	4	1, 7, 13, 9
10	Stomach	4	4	8, 1, 11, 7	2	3	8, 17, 18	9	8	4, 14, 15, 7, 13, 1, 9, 22
11	Abdomen	1	1	1	2	1	19	2	2	7, 14
12	Rectum, stool	2	3	20, 8, 7	3	3	8, 7, 19	5	3	9, 14, 15
13	Cough	3	2	11, 8	2	2	8, 17	3	3	4, 14, 15
14	Chest	1	1	16				3	1	1
15	Sleep	3	6	22, 15, 20, 14, 7, 18, 1	2	2	17, 19	3	7	1, 13, 7, 18, 4, 11, 2
16	Urinary organs	2	2	1, 7	–	–	–		2	1, 13
17	Urine	–	–	–	–	–	–		2	1, 13
18	Male genitals	–	–	–	–	–	–	1	1	7
19	Female genitals	–	–	–	–	–	–	4	3	4, 6, 1
20	Neck, back	1	1	16	4	1	8	7	6	11, 14, 1, 6, 15, 22
21	Extremities	4	4	1, 8, 6, 9	4	3	8, 17, 19	6	7	1, 4, 7, 11, 14, 18, 20
22	Fever	–	–	–	–	–	–	1	2	4, 14
23	Skin	3	4	15, 2, 13, 5	1	1	3	12	6	1, 4, 2, 5, 6, 7
24	Generals	1	2	8, 2	2	2	8, 17	5	7	1, 4, 18, 7, 6, 20, 15
	Total	47			30			135		
SPV	*SPV* = No. Symptoms/No. of volunteers*	–			30/7 = 4.28			135/15 = 9		

SPV = Symptoms per volunteer (Incidence of pathogenetic effects per volunteer).

for 1 day)] **Hair fall** (Number of volunteers: 2) (9^{+++}, 5^{++})

4. **Eyes: Burning and watering < evening** (Number of volunteers: 2) (6^{+}, 5^{++}) **Burning** (Number of volunteers: 3) [6^{+}, 5^{++}, 14^{++})
5. **Nose: Sneezing** (Number of volunteers: 3) (4^{++}, 9^{+++}), **Nose, watery discharge** (Number of volunteers: 3) (9^{+++}, 16^{+++}, 6^{+})
6. **Face: Acne** (Number of volunteers: 3) ($2^{++,}$ 9^{+}, 18^{+})
7. **Mouth:** Mouth, ulcer inner surface of lower lip, burning < while eating. (Number of volunteers: 1) (13^{+++})
8. **Teeth: Tooth pain** (Number of volunteers: 2) (7^{++}, 14^{+++})
9. **Throat: Throat, pain** (Number of volunteers: 3) (1^{+++}, 9^{+++}, 13^{+})
10. **Stomach: Appetite decreased** (Number of volunteers: 2) (4^{+}, 15^{++}) **Appetite increased** (Number of volunteers: 3) (7^{++}, 13^{++}, 16^{++++}) **Thirst decreased** (Number of volunteers: 2) (1^{+++}, 15^{++}) **Thirst increased.** (Number of volunteers: 3) [4^{++}, 9^{+++}, 13^{++}) **Acidity, burning in epigastric** (Number of volunteers: 3) (1^{++}, 15^{+++}, 22^{++})
11. **Abdomen:** Abdomen, flatulence < after eating. Heaviness (Number of volunteers: 1) [15^{++}]
12. **Rectum and stool: Stool, scanty, hard, unsatisfactory** (Number of volunteers: 3) (9^{+}, 15^{++}, 16^{++})
13. **Female sexual organs: Menses, painful** (Number of volunteers: 2)(4^{++}, 6^{++})
14. **Urinary organs: Urine, frequency increased** (Number of volunteers: 2) (1^{++}, 13^{+})
15. **Cough: Cough** (Number of volunteers: 3) ($4^{+++,}$ 15^{+}, 16^{++})
16. **Sleep: Drowsiness** (Number of volunteers: 4) (1^{+++}, 7^{++}, 13^{++}, 18^{++}) Sleep**, un-refreshing** (Number of volunteers: 2) (1^{+}, 13^{++})
17. **Extremities: Cramps, calf muscles** (Number of volunteers: 2) (4^{+}, 15^{++}) Pain **in left leg < half an hour**

No	*Drug proving symptoms*	*Hepatitis C disease symptoms*
1.	Reduced appetite(2 volunteers)	Loss of appetite
2.	Acidity, burning in epigastric(3 volunteers)	Gastritis, nausea
3.	Exhausted, weak feeling(5 volunteers)	Weakness, fatigue
4.	Pain in back, lumbar, lumbosacral(2 volunteers), pain in neck(2 volunteers),	Joint pain
5.	Pain in muscles(3 volunteers)	Muscle pain
6.	–	Weight loss
7.	–	Symptoms and signs associated with liver cirrhosis leading to portal hypertension, ascites, easy bruising or bleeding, varices; cancer, etc.

in morning. Pain in left arm and forearm, morning (Number of volunteers: 1) [20^{++++}]

18. **Neck: Neck, drawing pain in nape of neck < pressure, < flexion of neck.** (Number of volunteers: 1) [11^{++++}], **Pain in nape of the neck** (Number of volunteers: 2) (11^{+++}, 15^{++})
19. **Back: Pain in back, lumbar, lumbosacral** (Number of volunteers: 3) (6^{++}, 16^{++}, 22^{++})
20. **Fever: Fever or feverish** (Number of volunteers: 2) (4^{+++}, 14^{++})
21. **Skin: Head, papular eruptions, on forehead** (Number of volunteers: 2) (1^{++}, 4^{++}) **Acne on forehead, oily forehead skin.** (Number of volunteers: 1) [7^{++++}] **Skin rash, eruptions, itching** (different area like forehead, scalp, nape of the neck, forearms, abdomen, margins of hair) (Number of volunteers: 5) (1^{++}, 4^{++}, 5^{+++}, 6^{++}, 7^{++})
22. **Generalities: Body ache, body pain, all over** (Number of volunteers: 3) (1^{++}, 4^{++}, 18^{++}) Tiredness **all over body.** (Number of volunteers: 2) (15^{+}, 16^{++}) **Exhausted, weak feeling** (Number of volunteers: 5) [1^{+++}, 4^{++}, 7^{++}, 18^{+}, 20^{++})

Symptoms reported by volunteers compared with symptoms of hepatitis C

The symptoms undraped by Hep C drug proving has some thought-provoking similarity with the symptoms of Hep C disease; which is capable of arousing scientific curiosity as to how a potentized substance could produce symptoms without biological presence of the virus. The drug proving with potentized nosode, logically, would never produce changes such as hepatitis, cirrhosis, varices, thrombocytopenia, and the like; but can only show some signs of an ability to trigger certain processes, which need to be further examined.

Discussion

Hepatitis C nosode was produced from genotypes I and III; other genotypes can be explored in future. The double blind, placebo control method is a scientific process of homeopathic pathogenetic trial. Symptoms produced during the run in period (with placebo) were not considered if the volunteer continued to report the same symptoms, when on the medicine. This proved to be a powerful filter in eliminating placebo effect to a large extent. No drug proving data can be one hundred percent pure effect of the medicinal substance, as perceived by the investigator. The challenge lies in sieving the data by meticulous evaluation, elimination and analysis.

The inclusion of a placebo control group (N = 7) helped to compare the qualitative and quantitative form of the symptoms; and not as an additional filter; as exclusion of all the symptoms produced with placebo from the drug-produced symptom group (N = 15), is not logical. Only repeated drug proving could lower or possibly rule out unreliable symptoms in the proving, which cannot be disqualified from a single trial. Again, it must be remembered that multiple trials could lead to many more ambiguous symptoms. The homeopathic Pathogenetic trial has shown induced largely subjective symptoms, marginal changes in blood works and none in electrocardiograms. Scientifically speaking, skepticism could prevail in considering such subjective data as sole basis of prescription; which is true for large part of the data that we have in the materia medica, derived from less systematically documented drug proving.

It must be noted that the Hep C virus takes 10—25 years to produce symptoms. Most patients experience minimal or no symptoms during the initial stages of the infection.[14] Based on this fact, the homeopathic Pathogenetic trial with a potentized agent, cannot be expected to induce many symptoms in a short span of six weeks. Early symptoms of Hepatitis C are generally mild and vague, including a decreased appetite, fatigue, nausea, muscle or joint pains, and weight loss.[15]

This study has shown certain objective changes in SGOT, SGPT, serum alkaline phosphatase, total leukocyte count, and eosinophil count, but not sufficient to be conclusive.

Data received through the pathogenetic trial forms one of the sources of materia medica. In case of nosodes, knowledge of microbiology and that of the effects of the microbes has evolved so much that the most reliable source of the *deeper* effects of the microbial substance in question should be the clinical microbiology. The author would like to stress that the Hep C disease picture is a *form* of homeopathic Pathogenetic trial, revealing *effects* of the virus on humans; as the disease picture of Tuberculosis[16] is to Tuberculinum nosode.[17—20]

Some mental symptoms such as confusion, laziness, dullness, irritability and weeping were found in more than one volunteer. Symptoms such as irritability are rather vague; and very easy for any volunteer to exhibit. One volunteer (number 1) used the work 'melancholy' during run-in period; while 'sad' when on the drug; these were considered synonymous and not counted in the analysis. Dreams produced by some volunteers have not been considered significant; except the dream of snakes, since it was observed in three volunteers.

The study has proved higher incidence of pathogenetic effect per volunteer in verum group (9) as compared to the placebo group (4.28). This supports the observation by other researchers (Walach, *et al.*, 2009) that homeopathic remedies produce different symptoms than placebo.[6,7]

Placebo control with randomization and blinding excluded bias; confirming the capability of the ultramolecular homeopathic preparation to produce specific and relevant effect.

Conclusion

The nosode used in this study was prepared by a standardized and reproducible method. Double blind, placebo controlled pathogenetic trial of the Hep C nosode exposed symptoms, which will guide the use of this medicine in disease conditions, not limited to Hepatitis C. Homeopathic pathogenetic trial is not the only source of prescribing indications for any remedy and clinical verification is required. Hep C nosode needs to be evaluated for the cases of Chronic Hepatitis (infective, alcoholic, non-infective), cancer of liver, and related conditions.

Conflict of interest

The Hep C nosode preparation project and Hep C nosode pathogenetic trial project were sponsored by Homeopathy India Pvt Ltd. The method of production of the nosode is the subject of patent applications by the author. The sponsors had no role in data collection, analysis, and interpretation.

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.homp.2013.02.002.

References

1 Houghton M. The long and winding road leading to the identification of the hepatitis C virus. *Journal of Hepatology* November 2009; **51**(5): 939−948 http://dx.doi.org/10.1016/j.jhep.2009.08.004. PMID 19781804.
2 http://en.wikipedia.org/wiki/Hepatitis_C.
3 http://www.e-hepatitis-c.com/app/hepatitis-c.asp (March, 19, 2012).
4 http://www.ias.ac.in/jbiosci/nov2008/465.pdf (Page 468) (March, 19, 2012).
5 Alter MJ. Epidemiology of hepatitis C virus infection. *World Journal of Gastroenterology: WJG* 2007−05-07; **13**(17): 2436−2441. PMID 17552026. (March 18, 2012).
6 Möllinger H, Schneider R, Walach H. Homeopathic Pathogenetic Trials Produce Specific Symptoms Different from Placebo. *Forsch Komplementmed* 2009; **16**: 105−110.
7 Piltan D, Rist L, Simões-Wüst A, Saller R. Test of a homeopathic dilution of Aconitum napellus. A clinical, randomized, double-blind, controlled crossover study in healthy volunteers. *Forsch Komplementmed* 2009; **16**: 168−173.
8 http://www.homeopathyeurope.org/publications/guidelines/homeopathic-provings/ECH_Proving_Guidelines_v1.pdf, page 5 (2nd March, 2010).
9 Hahnemann S. *Organon of Medicine*. 6th edn. B. Jain Publishers, 1979. reprint, pages 190−212.
10 CCR Central Drug Proving Cum Data Processing Cell, and Pre and Post trial medical report proforma, CCRH, (year not specified), published by CCRH, Ministry of Health, New Delhi, India. http://ccrhindia.org/index.asp.
11 Indian Council of Medial Research, New Delhi. *Ethical Guidelines for Biomedical Research on Human Participants*, http://icmr.nic.in/ethical_guidelines.pdf; 2006.
12 http://ctri.nic.in (16th January, 2012).
13 Dantas F, Fisher P, Walach H, Wieland F, Rastogi DP, Teixeira H, Koster D, Jansen JP, Eizayaga J, Alvarez MEP, Marim M, Belon P, Weckx LLM. A systematic review of the quality of homeopathic pathogenetic trials published from 1945 to 1995. *Homeopathy* 2007; **96**: 4−16, http://www.clubdelarazon.org/downloads/homeopatia45-95.pdf (Downloaded 26th February, 2012).
14 Wilkins T, Malcolm JK, Raina D, Schade RR. Hepatitis C: diagnosis and treatment. *American Family Physician* 2010−06-01; **81**(11): 1351−1357. PMID 20521755 (March 17, 2012).
15 *Chronic Hepatitis C Virus Advances in Treatment, Promise for the Future*. Springer Verlag, ISBN 9781461411918; 2011 (March 17, 2012), pp. 103−104.
16 http://en.wikipedia.org/wiki/Mycobacterium_tuberculosis (16th January, 2012).
17 Hering C. The Guiding Symptoms of Our Materia Medica, Vol 10. B. Jain Publishers, 1989. reprint, page: 211, page: 350.
18 William Boericke. *Pocket Manual of Homoeopathic Materia Medica*. B. Jain Publishers, 1981. Export Edition, page: 655.
19 Sarkar BK. *Up-to-dates with Nosodes*. Roy Publishing House, 1971. page: 20.
20 Kent JT. *Lectures on homoeopathic Materia Medica*. Jain Publishing Co., 1980. reprint, page: 1001.