Original Article

Formic acid: A multicentric observational homoeopathic clinical verification trial

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Abstract

Aims: This study was done to clinically verify the symptomatology of *Formic acid* by ascertaining the symptoms improved during verification and to incorporate new findings (if any) to the known symptomatology of *Formic acid*. **Methods:** A multicentric observational clinical verification study was conducted at nine research centers of Central Council for Research in Homoeopathy to verify the proving symptoms of rarely used medicine, *Formic acid*. Two hundred and seventy participants having symptomatological similarity with *Formic acid* were included and prescribed in 6C, 30C, 200C, and 1M potencies, as per need of each case. The data were compiled in a specially designed Excel spreadsheet for further analysis. The collected data were presented in terms of descriptive statistics. Prevalence of the symptoms in the responding and nonresponding population was compared using Chi-square or Fisher's exact test. **Results:** Out of 266 followed up patients, 215 cases responded (80.8%) with 95% confidence interval of 0.75–0.85. The number of symptoms verified was as follows: proving symptoms ($n = 11$) and new observations ($n = 22$). The widely emerged new general symptoms, i.e., clean tongue, disturbed sleep, loose stool, tastelessness, and profuse sweat may be worth consideration during prescription of *Formic acid.* **Conclusions:** The proving symptoms of *Formic acid* could be verified clinically, but the correlation of patient-specific symptom needs cautious interpretation. Further replication on larger sample and estimation of likelihood ratio in real-time clinical practice are needed.

Key words: Arthritis, Clinical verification, Dyspepsia, *Formic acid*, Homoeopathy

Introduction

Evidence-based Homoeopathy is a challenge for future years. In evidence-based medicine, we are looking for proof of efficacy of treatments for specific diagnoses. Evidence-based Homoeopathy is concerned with clinical verification of symptoms used in homoeopathic practice. The organization of such verification is not simple since homoeopaths use different methodologies and strategies according to their training, expertise, and clinical experience.[1] An unconfirmed proving symptom that was never verified by clinical data cannot yet be considered useful for homoeopathic practice. The system must allow verification of symptoms from remedy proving as well as clinical symptoms which will never originate from pathogenetic trials alone.[2]

The aim of this paper is to generate an enhanced drug picture of lesser known drug, *Formic acid* by verifying its proving symptoms and by incorporating new findings (if any) in the symptomatology of *Formic acid*.

Formic acid (systematically known as methanoic acid)[3] was first used as a medicine by Mr. R. Wallace of Richmond, who described its usefulness in three letters sent to Anshutz.[4] It was recommended to the homoeopathic fraternity by Dr. John Henry Clarke for cases of varicose veins, polypi, and catarrh.[4,5] Since his time, no comprehensive study has

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been done to extend further the therapeutic utility. Assuming the clinical importance of the drug and keeping in mind the nonavailability of probable pathogenesis, a systematic proving of *Formic acid*, with randomized, double-blind, placebo-controlled technique was conducted by Central Council for Research in Homoeopathy (CCRH)[6] followed by its clinical verification to ascertain its therapeutic usefulness. Council took up its proving in 1980–1981 and after that verification was done by the council to enhance its therapeutic utility.

Description

Chemical symbol: HCOOH[7]

Mol. Wt.: 46.03[7]

Synonyms: English: *Formic acid*[7]

French: Acide formique[7]

German: Ameisensaure[7]

Formic acid is the simplest carboxylic acid.[3] It is a colorless liquid, having a pungent acid odor, and a burning taste; it crystallizes at 0°C and boils at 100°C; soluble in all proportions in water, alcohol, or glycerin. Its specific gravity is 1.23. When applied to the skin, it produces a burning sensation and even blisters.[7]

It is an important intermediate in chemical synthesis and occurs naturally, most famously in the venom of bee and ant stings. The principal use of *Formic acid* is as a preservative and antibacterial agent in livestock feed.[3] Metabolism of methanol, methyl ethers, esters, and amides gives rise to *Formic acid*. This acid is an inhibitor of the mitochondrial cytochrome oxidase causing histotoxic hypoxia.[8] This acid was first obtained by the distillation of ants, by Samuel Fisher (Lavoisier).[9]

Formic acid is found in certain caterpillars, and doubtless, the "*bombic acid,*" Lavoisier mentions as being obtained from silkworm larva, was impure *Formic acid*. Later, F. Will has shown that the fluid in the hairs of a species of caterpillar, which causes inflammation of the skin when handled and the poisoning by the sting of some insects, is due to the *Formic acid* present. It has also been demonstrated that the stinging hairs of the nettle, *Urtica urens,* and *Urtica dioica* contain this acid. *Formic acid* is also found in pine tree leaves and in the blood, bile, urine, perspiration, and muscular tissues of man.[9]

The place of *Formic acid* in medicine and chemistry is a great and growing one. In the form of tincture of ants, *Formica rufa*, has a distinct place in homoeopathic practice.[4] *Formic acid* in small doses increases muscular strength and resistance to fatigue. In prescribing, Clarke orders an ounce or two of a solution of *Formic acid* in the proportion of one part of the acid to eleven parts of distilled water. Of this, one teaspoonful is taken in a tablespoonful of water after food once or twice daily.[5] In cases of acute rheumatic fever and acute gonococcal arthritis, *Formic acid* 6X, 1 cc., every 6 days showed splendid results.[10]

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 study of *Formic acid* was started in June 2010 and continued until March 2014 at 9 research centers of CCRH across India.

Methods

Study Design

Multicentric observational clinical verification study was conducted at Central Research Institute, Noida (Uttar Pradesh), Homoeopathic Drug Research Institute, Lucknow (Uttar Pradesh), Regional Research Institute (H), Puri (Odisha), Regional Research Institute (H), Shimla (Himachal Pradesh), Regional Research Institute (H), Gudivada (Andhra Pradesh), Regional Research Institute (H), Imphal (Manipur), Dr. Anjali Chatterjee Regional Research Institute (H), Kolkata (West Bengal), Clinical Research Unit (H), Port Blair (Andaman and Nicobar Islands), and Clinical Verification Unit, Patna (Bihar) from June 2010 to March 2014.

Participants

Participants having symptomatological similarity *Formic acid* and from all age groups irrespective of sexes were included in the study. Exclusion criteria were clinical presentations not corresponding with the medicine and the patients who were on regular medication for any systemic disease. Patients who were on any medication for any "acute" purpose, 1 week before being enrolled in the study, were put on a washout period of 7 days. Informed written consent was obtained from the eligible patients or from the guardians in case of minors before initiating the study.

Data Sources/Measurement

At the baseline, the symptoms were repertorized using a repertory, prepared for this purpose by the council to aid the investigator in the selection of an appropriate medicine and subsequently confirmed from the Materia Medica. This was prepared specially for the study comprising the proving symptoms of the drug, to find out the similarity of *Formic acid* with the symptoms collected. *Formic acid* was prescribed according to the similarity of symptoms. Study medicine was procured from the licensed pharmacy in various potencies, namely 6C, 30C, 200C, and 1M.

Thus, if *Formic acid* was found indicated for the patient as per the drug picture recorded,[9] it was prescribed in 6C potency thrice a day. If it was not indicated, the patient was excluded from the study and treated in the general OPDs of the respective research institutes/units. The changes in presenting

symptoms and signs were recorded during the follow-up visits. If there was any kind of improvement, medicine was stopped and was followed by placebo. If there was no change in symptoms and signs even up to 7 days, the next higher potencies such as 30C, 200C and 1M were prescribed as per the need of the case and in accordance with homoeopathic principles. If no change was observed even after the change of potencies, the case was closed and considered as a clinical failure.

Sample Size

A total of 6210 patients were screened from the OPDs of nine centers of CCRH. Out of this, 5940 cases who did not meet the inclusion criteria were excluded from the study. Two hundred and seventy patients were enrolled having similar symptomatology with *Formic acid* and meeting the prespecified eligibility criteria. Of these, four dropped out and 266 cases were analyzed [Figure 1].

Statistical Method

The data of all the cases were collected and compiled in specially designed Excel spreadsheet and thereafter analyzed. Data were presented in number, percentage, mean, and standard deviation. Prevalence of the symptoms in the responding and nonresponding population was compared using Chi-square or Fisher's exact test, keeping $P < 0.05$ two-tailed as statistically significant. As per protocol a minimum of two prescriptions for each symptom has been considered for enlisting.

Results

A total of 270 patients were enrolled having similar symptomatology with *Formic acid* and meeting the prespecified eligibility criteria. Of these, four dropped out and 266 results were analyzed in the end [Figure 1].

Among the enrolled patients, 137 (51.5%) were male, rest of 129 (48.4%) were female. The mean age in years of the patients was 35.0 ± 13.2. Mean body mass index (BMI) was 23.2 ± 3.10, and most of the patients (n = 195, 74%) belonged to the normal BMI range of 18.5–24.9. Two hundred and fifty-one (94%) were married and the majority (n = 110, 44%) were homemaker [Table 1].

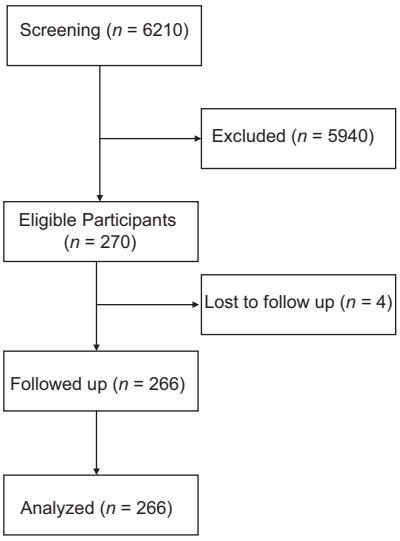

Figure 1: The study flow diagram

Out of 266 registered cases, 215 cases (80.8%) responded to *Formic acid*. The clinically verified symptoms were enlisted along with the outcomes on the basis of proving records (drug proving profile generated by CCRH) and the symptoms available in other literature and also the new observations (clinical symptoms), those are not mentioned elsewhere but found to have improved after the administration of *Formic acid* [Table 2].

Among 215 patients, a total of six different clinical diagnoses were obtained. Dyspepsia was the most frequently diagnosed condition (n = 166, 62.05%) followed by headache (n = 127, 47%) and followed by arthralgia (n = 115, 43.2%) [Table 3].

Among the proving and clinically verified symptoms, most frequently observed were:

- Diminished appetite (n = 199, prevalence 92.55%, confidence interval [CI]: 87.98, 95.55)
- Dull pain in right hypochondrium; < by motion and > by lying down (n = 166, prevalence 76.27% in responding group, 95% CI: 69.92–81.68)
- Heaviness of head in morning from 6.30 a.m. to 8.00 a.m. (n = 131, prevalence 59.06% in responding group, 95% CI: 52.16, 65.65)
- Pain in left leg as if sprained (n = 120, 53.95% prevalence in responding group, 95% CI: 47.05–60.71)
- Desire for onions (n = 82, 38.13% prevalence in responding group, 95% CI: 31.69–45.02)
- Diminished thirst was observed in 69 patients in responding group with 32.09% prevalence and 95% CI: 25.99, 38.84
- Sixty-seven cases of yellow coated tongue were observed in responding group (31.16% prevalence, CI: 25.13, 37.88
- Nocturnal seminal emissions without dreams, followed by weakness (n = 48, 22.32% prevalence in responding group, 95% CI: 17.17, 28.60)
- Cramp-like pain in lower abdomen before menstruation, better after onset of menstrual flow (n = 31, 14.41% prevalence in responding group, 95% CI: 10.15–20.0) [Table 2].

Among the newly observed symptoms, patients who responded positively were either chilly (n = 74, 34.4% prevalence in responding population, 95% CI: 28.14–41.23) or sensitive to both extremes (n = 66, 24.18% prevalence in responding population, 95% CI: 24.7–37.4). Most widely obtained symptoms were:

- "Clean tongue" (n = 20, 9.30% prevalence in responding population, 95% CI: 5.91, 14.20)
- "Disturbed sleep" (n = 16, 7.4% prevalence in responding population, 95% CI: 4.45, 12.02)

Table 1: Baseline information (*n*=266)

Characteristic	*n* (%)
Gender (*n*=266)	
Male	137 (51.5)
Female	129 (48.4)
Age (years) (*n*=266)	35.0±13.2
≤18	16 (6.0)
19-30	85 (32.0)
31-50	129 (48.4)
51-70	34 (12.7)
≥71	2 (0.75)
Religion (*n*=266)	
Hindu	251 (94)
Muslim	13 (4.8)
Marital status (*n*=254)	
Married	197 (77.5)
Unmarried	57 (22.4)
Occupation (*n*=250)	
Homemaker	110 (44)
Student	45 (18)
Service	39 (15.6)
Business	10 (4)
Others	46 (18.4)
BMI: Mean±SD	23.2±3.1
BMI (*n*=263)	
Underweight (<18.5)	15 (5.7)
Normal (18.5-24.9)	195 (74)
Overweight (25-29.9)	44 (16.7)
Obese I (30-34.9)	6 (2.2)
Obese II (35-39.9)	3 (1.1)

SD: Standard deviation; BMI: Body mass index

- "Loose stool" (*n* = 14, 6.5%, 95% CI: 3.74, 10.91)
- Tastelessness was noticed in 13 patients (6.04% prevalence) in responding group, 95% CI: 3.4, 10.36
- "Profuse sweat" (*n* = 9, 4.1 prevalence in responding population, 95% CI: 2.06, 8.06); [Table 2].

Significantly higher prevalence of the symptoms under question in the responding population than in the nonresponding population was found in case of five symptoms:

1. Heaviness of head in the morning from 6.30 a.m. to 8.00 a.m. with chilliness (127/215 vs. 04/51; Chi-square (Yates corrected) =41.25; *P* = 0.001 two-tailed)
2. Dull pain in right hypochondrium; < by motion and > by lying down (164/215 vs. 02/51; Chi-square (Yates corrected) =88.93; *P* = 0.001 two-tailed)
3. Nocturnal seminal emissions without dreams, followed by weakness (48/215 vs. 03/51; Chi-square (Yates corrected) = 6.17; *P* = 0.01 two-tailed)
4. Pain in left leg as if sprained (116/215 vs. 04/51; Chi-square (Yates corrected) =33.5; *P* = 0.001 two-tailed)
5. Chilly patient (74/215 vs. 13/51; Chi-square (Yates corrected) = 1.11; *P* = 0.29 two-tailed)
6. Easily angered (10/215 vs. 02/51; Chi-square (Yates corrected) = 0.05; *P* = 0.82 two-tailed).

However, as far as the peculiarity of the symptoms, according to their prevalence in responding population, are considered, the first five may be segregated further and may be deemed as the most promising symptoms for future research [Table 4].

Discussion

During this study, eleven symptoms of *Formic acid* were verified, which were from the proving of the medicine conducted by the Council. Alongside, some new symptoms were identified as clinically associated symptoms, improved wholly or partially, or showing improvement in the main complaint. Many symptoms showed improvement of 75% or higher [Table 2].

The main spheres of action of *Formic acid* were head, stomach, abdomen, male genitalia, female genitalia, and extremities. Most frequently encountered clinical conditions found to be improved were dyspepsia (164 improved out of 166), headache (127/131), arthritis (108/115), spermatorrhea (42/58), varicose veins (17/19), and lipoma (3/8). Apart from these conditions, *Formic acid* showed improvement in cases of dysmenorrhea, menorrhagia, amebiasis, and lymphadenitis also.

Formic acid, though belonging to one of the major group (acid group) of homoeopathic medicines, has always remained a lesser known and lesser used drug. Traditionally, also *Formic acid* was rarely employed as a medicine; it was only used externally as a local irritant, in sluggish capillary circulation, in certain painful affections, and in enfeebled or paralytic conditions of the limbs.

Homoeopathically, it was used by John Henry Clarke in treating cases of chronic arthritis successfully. In spite of this, *Formic acid* still remained a lesser known drug. Our study confirmed its use in cases of arthritis once again. Along with this, our study shows that it may also be used in other conditions such as dyspepsia, headache, and spermatorrhea as a good number of patients of these conditions were found to be improved by this medicine. Strikingly, all the 19 patients (100%) suffering from varicose veins improved after treatment. Apart from this, the newly emerged general symptoms may offer promising help while considering prescribing *Formic acid*. These findings are probable and need confirmation through clinical observations.

The action of *Formic acid* on extremities was marked with symptoms such as pain in the left leg as if sprained, thus confirming one of the symptoms available in literature, i.e., varicose veins in the left leg. Besides this, some symptoms such as heaviness of head in the morning from 6.30 a.m. to 8.00 a.m., heaviness in abdomen, dull pain in right hypochondrium, flatulence at night, desire for onions, yellow coated tongue, and nocturnal seminal emissions emerged as important pathogenesis of *Formic acid*. Statistical significance in these symptoms increases the probability of the drug in curing such illness in clinical practices. Moreover, this study

Table 2: List of symptoms verified

Symptoms (CCRH Proving)[6]	Symptom prevalence (%) in medicine population (*n*=266)	95% CI	Symptom prevalence (%) in responding population (*n*=215)	95% CI	Symptom prevalence (%) in not responding population (*n*=51)	95% CI	Chi square value at df=1 (Yates corrected)	*P*
Heaviness of head in the morning from 6.30 a.m.-8.00 a.m. with chilliness	131 (49.2)	43.1-55.4	127 (59.0)	52.1- 65.6	04 (7.8)	2.5-19.7	41.2	0.001*
Tongue yellow coated	99 (37.2)	31.6-43.1	67 (31.1)	25.1-37.8	32 (62.7)	48-75.5	16.2	0.001*
Diminished appetite	240 (90.2)	85.8-93.4	199 (92.5)	87.9-95.5	41 (80.3)	66.4-89.7	5.6	0.01*
Diminished thirst	92 (34.5)	28.9-40.6	69 (32)	25.9-38.8	23 (45)	31.3-59.5	2.5	0.11
Desire for onions	95 (36)	30-41.8	82 (38.1)	31.6-45	13 (25.4)	14.7-39.9	88.9	0.12
Heaviness in the abdomen with flatulence.	141 (53.4)	46.8-59.1	128 (59.5)	52.6-66	13 (25.4)	14.7-39.9	17.8	0.001*
Offensive stool	141 (53.4)	46.8-59.1	128 (59.5)	52.6-66	13 (25.4)	14.7-39.9	17.8	0.001*
Dull pain in right hypochondrium; < by motion and > by lying down	166 (62.4)	56.2-68.1	164 (76.2)	69.9-81.6	02 (3.9)	0.6-14.5	88.9	0.001*
Nocturnal seminal emissions without dreams, followed by weakness	51 (19.1)	14.8-24.3	48 (22.3)	17.1-28.6	03 (5.8)	1.5-17.2	6.1	0.01*
Pain, cramp-like, in lower abdomen before menstruation, better after onset of menstrual flow.	33 (12.4)	8.9-16.9	31 (14.4)	10.1-20	02 (3.9)	0.6-14.5	3.2	0.07
Pain in the left leg, as if sprained	120 (45.1)	39-51.3	116 (53.9)	47-60.7	4 (7.8)	2.5-19.7	33.5	0.001*
Symptoms/New observations								
Thermal relations								
Hot patients	21 (7.8)	5.0-11.7	15 (6.9)	4.1-11.4	6 (11.7)	4.8-24.5	0.7	0.39
Chilly patients	87 (32.7)	27.1-38.7	74 (34.4)	28.1-41.2	13 (25.4)	14.7-39.9	1.1	0.29
Sensitive to extremes	85 (31.9)	26.4-37.9	66 (24.8)	24.7-37.4	19 (37.2)	24.4-51.9	0.5	0.46
Desire/craving for food/drink								
Salty	12 (4.5)	2.4-7.9	7 (3.2)	1.4-6.8	5 (9.8)	3.6-22.1	2.7	0.09
Spicy	11 (4.1)	2.1-7.4	10 (4.6)	2.3-8.6	1 (1.9)	0.1-11.7	0.2	0.63
Sweets	9 (3.3)	1.6-6.5	6 (2.7)	1.1-6.2	3 (5.8)	1.5-17.2	0.4	0.50
Sour	6 (2.2)	0.9-5.0	5 (2.3)	0.8-5.6	1 (1.9)	0.1-11.7	0.0	0.87
Aversion/dislike to food/drink								
Milk	5 (1.8)	0.6-4.5	5 (2.3)	0.8-5.6	0 (0)	0-8.7	0.2	0.59
Sweets	4 (1.5)	0.4-4.0	4 (1.8)	0.6-5.0	0 (0)	0-8.7	0.1	0.72
Thirst								
Increased	13 (4.8)	2.7-15.4	7 (3.2)	1.4-6.8	6 (11.7)	4.8-24.5	4.7	0.02*
Tongue								
White	6 (2.2)	0.9-5.0	4 (1.8)	0.6-5.0	2 (3.9)	0.6-14.5	0.1	0.71
Clean	29 (10.9)	7.5-15.4	20 (9.3)	5.9-14.2	9 (17.6)	5.5-23.3	2.1	0.14
Taste								
Bitter	8 (3.0)	1.4-6.0	6 (2.7)	1.1-6.2	2 (3.9)	0.6-14.5	0.1	0.67
Tasteless	15 (5.6)	3.3-9.3	13 (6.0)	3.4-10.3	2 (3.9)	0.6-14.5	0.06	0.79
Stool								
loose	29 (10.9)	7.5-15.4	15 (6.9)	3.7-10.9	14 (27.4)	17.9-44.0	19.9	0.001*
Urine								
Burning	3 (1.12)	0.2-3.5	3 (1.3)	0.3-4.3	0 (0)	0-8.73	0.01	0.91

Contd...

Table 2: Contd...

Symptoms/New observations	Symptom prevalence (%) in medicine population (*n*=266)	95% CI	Symptom prevalence (%) in responding population (*n*=215)	95% CI	Symptom prevalence (%) in not responding population (*n*=51)	95% CI	Chi square value at df=1 (Yates corrected)	*P*
Sweat								
Profuse	11 (4.13)	2.1-7.45	9 (4.1)	2.0-8.0	2 (3.9)	0.6-14.5	0.007	0.93
Sleep								
Disturbed	23 (8.6)	5.68-12.8	16 (7.4)	4.4-12.0	7 (13.7)	6.1-26.8	1.34	0.24
Dream								
Frightful	3 (1.12)	0.29-3.54	2 (0.93)	00.16-3.68	1 (1.96)	0.1-11.79	0.39	0.53
Mind								
Irritable	12 (4.5)	2.4-7.9	9 (4.1)	2.0-8.0	3 (5.8)	1.5-17.2	0.02	0.88
Easily angered	12 (4.5)	2.4-7.9	10 (4.6)	2.3-8.6	2 (3.9)	0.6-14.5	0.05	0.82
Brooding	3 (1.1)	0.2-3.5	3 (1.3)	0.3-4.3	0 (0)	0-8.73	0.01	0.911

[i]As per protocol a minimum of two prescriptions for each symptom have been considered for enlisting. CI: Confidence interval; CCRH: Central Council for Research in Homoeopathy;*P<0.05 Statistically Significant

Table 3: Clinical diagnoses

Clinical diagnoses[¥]	Number of patients (%)	95% CI
Dyspepsia	166 (62.1)	56.2, 68.1
Headache	131 (48.5)	43.1,55.4
Arthritis	115 (43.2)	37.2,49.4
Spermatorrhoea	58 (21.8)	17,27.3
Varicose veins	19 (7.14)	4.4,11.1
Lipoma	8 (3.0)	1.4,6.0

[¥]Conditions with a minimum of 5 diagnoses have been listed in this table. Total diagnoses do not reflect total number of patients because the patients presented with multimorbid conditions. Other diagnoses were dysmenorrhoea, menorrhagia, amoebiasis and lymphadenitis

Table 4: Promising symptoms for future research

Heaviness of head in the morning from 6.30 a.m. to 8.00 a.m. with chilliness
Dull pain in right hypochondrium; < by motion and > by lying down
Nocturnal seminal emissions without dreams, followed by weakness
Pain in the left leg as if sprained
Chilly patient

also confirms the use of *Formic acid* in helping cases of chronic arthritis.

Apart from the above observations, a group of valuable symptoms also emerged reflecting the picture of the drug and thereby widening the probable scope of its therapeutic applicability. Those were loose stool, desire for spicy things, clean tongue, tastelessness, profuse sweat, and disturbed sleep. As regards thermal modality, most of the patients were found to be either chilly or sensitive to extremes. Obtained mental features were irritability and easily angered. These may be considered as useful clinical concomitants, to prescribe the medicine. Moreover, the overall results generated were contributed by different study sites, indicating enhanced generalizability of the study findings. However, being an observational trial, this study cannot address the threats to various external and internal validity issues. Several weaknesses should be taken into account when considering the results of this research. Several sources of bias could influence the findings. In a retrospective work of this kind, it is quite difficult to assess when a patient has had a positive evolution, and it is much more difficult to attribute it to the treatment.[11]

Another possible source of bias is the difficulty in assessing the presence of symptoms in patients' records because the mere mention of the symptoms in them does not mean necessarily that they were really present in the patients nor that they were strong enough to be considered as medicine indicators.[11] Furthermore, we compared between responding and nonresponding patients for one medicine. This way, we can only get some idea of symptoms that can be further investigated. These could be of great value when compared with similar data of other medicines. However, the prevalence of symptoms should preferably be compared with the whole population.

The research protocol should have anticipated and kept provision to address the issues related to spontaneous recovery of the symptoms under question, for example, using modified Naranjo criteria. However, this observational trial, being exploratory in nature, cannot evaluate the same. Therefore, assessment of likelihood ratio (LR) of symptoms to be used as a rational means for detecting indicators to homoeopathic medicines. Prospective multicenter research of real prevalence and LR of symptoms should be carried out on to tune homoeopathic medicines' knowledge and more important, to improve prescription accuracy and clinical results.[11]

Conclusions

This study was conducted to clinically verify the "symptomatology" of *Formic acid* by ascertaining the symptoms improved during verification. This paper generated a list of clinically verified symptoms of *Formic acid* and warrants further evaluation using enhanced methodological rigor. On many occasions, a limited number of prescriptions was

generated for specific symptoms making interpretation difficult. For clinical data, the improvement should consist of using data from prospective, multicentered research. The symptoms with low prevalence need a greater number of cases to establish substantial LR. The implementation of LR indicating the increase (or decrease) of the likelihood that a medicine will be effective if a certain symptom is present (or absent).[12] The use of LR leaves less room for speculation and will enable more accurate and quantitative description of strength of the probable or claimed characteristic symptoms of the drug, based on empirical evidence instead of assumption. However, all these results should be considered as provisory and need confirmation through prospective research of real prevalence to the knowledge of medicines and more importantly, to increase posterior chance of correct selection of medicine, improve prescription accuracy and clinical outcomes. The causal association can be tested prospectively and systematically in all cases using modified Naranjo criteria in future studies.

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Conflicts of Interest

There are no conflicts of interest.

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Ameisensäure: Eine empirische Multi-Center-Studie klinischer Verifikationen

ZUSAMMENFASSUNG

Ziel: Diese Studie wurde durchgeführt, um die Symptomatik von *Formicum acidum* zu verifizieren, damit die bei der Verifikation ermittelten gebesserten Symptome und neue Ergebnisse (falls vorhanden) in die Symptomatologie von *Formicum acidum* aufgenommen werden.

Methode: Eine empirische Multi-Center-Studie wurde in neun Forschungszentren des „Central Council for Research in Homeopathy" (CCRH) zur Verifikation der Prüfungssymptome der selten genutzten Arznei *Formicum acidum* durchgeführt. 270 Teilnehmern mit einer Symptomenähnlichkeitsbeziehung zu *Formicum acidum* wurde es in C6, C30, C200 und 1M Potenzen, je nach Notwendigkeit, verabreicht. Die erhobenen Daten wurden in eine speziellen Excel Datei zur weiteren Analyse gebracht. Die gesammelten Ergebnisse wurden in einer deskriptiven Statistik vorgestellt. Die Verteilung der reagierenden und nicht-reagierenden Population wurde mit entsprechendem Chi-Quadrat-Test oder dem exakten Fischer-Test durchgeführt.

Ergebnisse: Von 266 Follow-up Patienten sprachen 215 (80,8%) mit einem Konfidenzintervall von 95%. Die Anzahl der verifizierten Symptome ist folgende: Prüfungssymptome (*n*=11) und neue Beobachtungen (*n*=22). Die neu aufgetretenen generellen Symptome sollten bei Verschreibungen berücksichtigt werden.

Fazit: Die Prüfungssymptome von *Formicum acidum* sollten klinisch verifiziert werden, wobei die Korrelation patientenspezifischer Symptome vorsichtig interpretiert werden müssen. Eine weitere Replikation und Wahrscheinlichkeitsschätzung an größeren Testgruppen in realer Zeit und unter klinischen Bedingungen sind weiter notwendig.

***Formicum acidum*: Estudio clínico, observacional, multicéntrico de verificación homeopática**

RESUMEN

Objetivos: Este estudio se ha realizado para verificar clínicamente la sintomatología de *Formicum acidum* y determinar los síntomas que mejoraron durante la verificación. El objetivo es incorporar los nuevos hallazgos (si se obtuvieran) en la sintomatología de *Formicum acidum*.

Métodos: Se ha realizado un estudio clínico, observacional, multicéntrico de verificación homeopática en nueve centros del CCRH (*Central Council for Research in Homeopathy*) para verificar los síntomas dpatogenésicos de un medicamento poco utilizado, el *Formicum acidum*. Se incluyeron 270 participantes que tenían una sintomatología similar al *Formicum acidum*, que se prescribió en las potencias de 6C, 30C, 200C y1M, en función de las necesidades de cada caso. Los datos se recogieron en una hoja de cálculo EXCEL especialmente diseñada para su posterior análisis. Los datos recogidos se presentaron con estadísticas descriptivas. La prevalencia de los síntomas en la población de respondedores y no respondedores se comparó con la prueba de chi cuadrado o la prueba exacta de Fisher.

Resultados: De los 266 pacientes con seguimiento, 215 casos respondieron (80,8%) con un intervalo de confianza el 95% de 0,75 a 0,85. El número de síntomas verificados fue el siguiente: síntomas de patogenesias (*n* = 11) y observaciones clínicas nuevas (*n* = 22). Los nuevos síntomas generales que surgieron han de considerarse en las prescripciones de *Formicum acidum*.

Conclusiones: Se han podido verificar clínicamente los síntomas de la patogenesia de *Formicum acidum*, pero es necesario interpretar con precaución la correlación de los síntomas específicos del paciente. Es esencial replicar estos estudios con una muestra más grande y estimar la relación de probabilidad en la práctica clínica real.

फार्मिक एसिडः एक बहुकेंद्रिक विश्लेषणात्मक होम्योपैथिक नैदानिक सत्यापन परीक्षण

सार

उद्देश्यः लक्षणों के सत्यापन के दौरान हुए सुधार के माध्यम से यह अध्ययन फार्मिक एसिड के चिकित्सकीय लक्षणों को सत्यापित करने के लिए और फार्मिक एसिड में नए निष्कर्षों को शामिल करने के लिए (अगर कोई है) किया गया।

पद्धतिः शायद ही कभी इस्तेमाल की जाने वाली औषधि, फार्मिक एसिड के नैदानिक लक्षणों को सत्यापित करने हेतु केन्द्रीय होम्योपैथी अनुसंधान परिषद् (सीसीआरएच) द्वारा नौ अनुसंधान केन्द्रों पर बहुकेंद्रिक, विश्लेषणात्मक होम्योपैथिक नैदानिक सत्यापन अध्ययन किया गया। फार्मिक एसिड के लाक्षणिक समानता वाले ऐसे दो सौसत्तर (270) प्रतिभागियों को शामिल किया गया। रोगी की आवश्यकता के अनुसार 6सी, 30सी में 200 सी और 1 एम पोटेंसीज की दवा दी गयी। आंकड़ों को आगामी विश्लेषण के लिए एक विशेष रूप से डिजाइन की गयी एक्सेल स्प्रेड शीट में संकलित किया गया। एकत्र किए गए आंकड़े विवरणात्मक सांख्यिकी के रूप में प्रस्तुत किए गए। अनुकूल और प्रतिकूल जनसंख्या में इन लक्षणों की व्यापकता की तुलना ची–वर्ग या फिशर सटीक परीक्षण का उपयोग करते हुए की गयी।

परिणामः 266 रोगियों में से 215 मामलों (80.8 प्रतिशत) में 0.75 से 0.85 के 95 प्रतिशत विश्वास अंतराल के साथ प्रतिक्रिया पायी गयी। सत्यापित लक्षणों की संख्या इस प्रकार रहीः प्रमाणित लक्षण (एन = 11) और नए नैदानिक विश्लेषण (एन = 22)। नवीन रूप से उभरे सामान्य लक्षणों जैसे साफ जीभ, अनिद्रा, दस्त, नीरसता और विपुल पसीना के आधार पर फोर्मिक एसिड पर औषधि निर्धारण के दौरान विचार हो सकता है।

निष्कर्षः चिकित्सकीय तौर पर फार्मिक एसिड के प्रमाणित लक्षण सत्यापित किए जा सकते है लेकिन मरीज के विशिष्ट लक्षण से परस्पर संबंध होने के कारण सतर्क व्याख्या की आवश्यकता है। इसके अलावा वास्तविक नैदानिक अभ्यास के दौरान बडे नमूनों पर प्रतिकृति और संभाव्य अनुपात का अनुमान महत्व रखता है।