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# Efficacy of Arsenicum album 30cH in preventing febrile episodes following DPT-HepB-Polio vaccination – a randomized, double-blind, placebo-controlled clinical trial

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ABSTRACT

*Background:* Among the post-immunization adverse events, especially of Diphtheria-Pertusis-Tetanus (DPT), fever is a common systemic reaction. There is anecdotal support for the use of the homeopathic medicine Arsenicum album in preventing post-vaccination fever. The investigators intended to evaluate its efficacy in preventing febrile episodes following vaccination.

*Methods:* In the community medicine out-patient of Mahesh Bhattacharyya Homoeopathic Medical College and Hospital, West Bengal, India, between August 2014 and January 2017, a double-blind, randomized, placebo-controlled trial was conducted on 120 children (verum: 60, placebo: 60) who presented for the 2nd and 3rd dose of DPT-HepB-Polio vaccination and reported febrile episodes following the 1st dose. Intervention used was Arsenicum album 30cH 6 doses or placebo (indistinguishable from verum), thrice daily for two subsequent days. Parents were advised to report any event of febrile attacks within 48 h of vaccination, either directly or over telephone.

*Results:* The groups were comparable at baseline. Children reporting fever after the 2nd dose was 29.8% and 30.4% respectively for the homeopathy group and control group respectively [Relative Risk (RR) = 1.008] with no significant difference ($P = 0.951$) between groups. Again after the 3rd dose, children reporting fever were 31.5% and 28.3% respectively for the homeopathy group and control group respectively (RR = 0.956) with no significant difference ($P = 0.719$) between groups.

*Conclusion:* Empirically selected Arsenicum album 30cH could not produce differentiable effect from placebo in preventing febrile episodes following DPT-HepB-Polio vaccination. [Trial registration: CTRI/2017/02/007939]

## 1. Introduction

Under the National Immunization Schedule in IndiaDiphtheria-Pertusis-Tetanus (DPT) Hepatitis B and Oral Polio Vaccine (OPV) are administered to the child simultaneously at the 6th (1st dose) 10th (2nd dose) and 14th week (3rd dose). Among the adverse events following immunization (AEFI) especially of DPT (Diphtheria-Pertusis-Tetanus) fever is a common systemic reaction.[1–3] 'Homeoprophylaxis' is gaining

*Abbreviations:* AEFI, adverse events following immunization; cH, Centesimal scale of hahnemann; CTRI, Clinical trials registry–India; DPT, Diphtheria-pertusis-tetanus; HepB, Hepatitis B; OPV, Oral polio vaccine; RR, Risk ratio

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popularity gradually in different countries; however the role of homeopathy in preventing AEFI has not been tested rigorously. There are anecdotal evidences in support of the homeopathic medicine Arsenicum album in curing fever arising as a consequence of inoculation, olfaction or ingestion of decayed food or animal matters into the body,[7] and even mentioned in literature about its usefulness in bad effects of vaccination.[8–11] howeverits efficacy in preventing febrile episodes following vaccination has not been investigated to date. ; This study tested whether Arsenicum album 30cHcould produce any significant effect beyond placebo in preventing febrile episodes following DPT-HepB-Polio vaccination given under National Immunization Schedule at 10th (2nd dose) and 14th week (3rd dose). We hypothesized that Arsenicum album 30cH could produce significant effect beyond placebo in preventing febrile episodes following DPT-HepB-Polio vaccination (Alternative hypothesis: HA) whereas Arsenicum album 30cH does not have any significant effect beyond placebo in preventing febrile episodes following DPT vaccination (Null hypothesis: H0).

This study tested whether Arsenicum album 30cH, could produce any significant effect beyond placebo in preventing febrile episodes following DPT-HepB-Polio vaccination, given under National Immunization Schedule at 10th (2nd dose) and 14th week (3rd dose). We hypothesized that Arsenicum album 30cH could produce significant effect beyond placebo in preventing febrile episodes following DPT-HepB-Polio vaccination (Alternative hypothesis: HA), whereas Arsenicum album 30cH does not have any significant effect beyond placebo in preventing febrile episodes following DPT vaccination (Null hypothesis: H0).

## 2. Methods

### 2.1. Trial design

This prospective, double-blind, randomized, placebo-controlled, parallel arm trial was conducted in the Community Medicine Out-patient of Mahesh Bhattacharyya Homoeopathic Medical College and Hospital. The study protocol was submitted and approved by the Institutional Ethics Committee [32/MBHMCH/CH/ADM/PRIN/17] and was registered subsequently in the Clinical Trials Registry – India [CTRI/2017/02/007939].

### 2.2. Participants

Inclusion criteria were the children aged 2.5–3.5 months and of both sexes, coming for the 2nd or 3rd dose of DPT-HepB-Polio having history of febrile episodes following first dose, and guardians' written consent to participate. Exclusion criteria were concurrent presence of other systemic or infectious disease, currently receiving homeopathic treatment, and self-reported immune-compromised state.

### 2.3. Intervention

In the intervention arm, Arsenicum album 30cH 6 doses were given, thrice daily for 2 days; each dose consisted of 4 cane sugar globules no. 30 medicated with a single drop of homeopathic medicine Arsenicum album 30cH preserved in 88% v/v ethanol [Batch no. 0324, mfg. Oct 2013, prepared from Arsenic trioxide 99.8% pure; quality control test report no. 3872/1997, dated Dec. 1, 1997; Hahnemann Publishing Co. Pvt. Ltd. (HAPCO)®]. In the control arm, identical placebo (indistinguishable from verum by appearance, smell, and taste) 6 doses were given, thrice daily for 2 days; each dose consisted of 4 cane sugar globules no. 30 moistened with a single drop of rectified spirit; indistinguishable from verum. Two of the investigators hold masters degree in homeopathy (recognized by Govt. of India and Govt. of West Bengal), and had more than 17 years of institutional practice and teaching experience.

### 2.4. Outcomes

Parent reported events of febrile attacks within 48 h of vaccination; either directly or over telephone was taken as the outcome measure.

### 2.5. Sample size

Absence of any controlled trial of similar design precluded calculation of standardized difference (effect size) and sample size. Hence, keeping $\alpha = 0.05$ and $\beta = 0.80$, as a rule of thumb, sample size of 100 seemed to be adequate[12] Keeping a provision for 20% drop-outs, target sample size became 120 (i.e. verum: 60, placebo: 60).

### 2.6. Randomization

Computer generated random number list were used to generate random sequence. The list was generated using restricted 12 blocks of size 10 ($n = 10$) to maintain equal distribution between groups and 1:1 ratio easily. Sequentially numbered identical coded containers were used for allocation concealment. Generation of random number chart and allocation codes was done in strict confidentiality by third party (SS and MK) who were not allowed to influence the study in any way.

### 2.7. Blinding

The participants and the investigators were blinded to the allocated codes. Codes were broken at the end of the trial after the data set was frozen.

### 2.8. Statistical methods

Per-protocol population was subjected to statistical analysis. The two groups were compared for baseline differences. Proportion of events (febrile episodes following DPT-HepB-Polio vaccination) occurring in the two groups was compared using chi-square test and *P* values less than 0.05 for a two-tailed test was considered as statistically significant. Reporting adhered to CONSORT[13] guidelines for reporting trials.

## 3. Results

### 3.1. Participant flow

In this study, 120 children were enrolled. Data after the 2nd and 3rd doses could not be collected for 7 (verum: 3, placebo: 4) and 6 (verum: 3, placebo: 3) participants respectively; i.e. total 13 patients dropped out (total 7 in the first phase and 6 in the second phase). (Fig. 1)

### 3.2. Recruitment

Starting from August 2014 until January 2017, total 120 children were enrolled in the study.

### 3.3. Baseline data

The two groups were comparable as per baseline characteristics, i.e. no significant baseline differences existed between groups in terms of gender distribution [$\chi^2 = 0.302$; $P = 0.583$], age [$t = 0.783$; $P = 0.436$], birth weight [$t = 1.210$; $P = 0.229$] and current body weight [$t = -0.152$; $P = 0.880$]. (Table 1)

### 3.4. Numbers analyzed

For the 2nd occasion of vaccination, outcomes from 57/60 and 56/60 children from the verum and placebo groups were analyzed respectively. And for the 3rd occasion, 54/60 and 53/60 responses were