A Prospective Multicentric Observational Study to Determine the Usefulness of Predefined Homoeopathic Medicines In the Management of Acute Diarrheal Disease in Children

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Abstract

Background & objectives: Acute diarrheal disease is one of the major causes of morbidity and mortality in developing countries. No data regarding the pediatric population suffering from acute diarrhea seeking homoeopathic treatment in India are available. Therefore, an observational study on acute diarrheal diseases in children was undertaken with fourteen predefined trial homoeopathic medicines in an effort to identify a group of homeopathic medicines useful for the treatment of acute childhood diarrhea.

Methods: A prospective, multi-center observational study was conducted by the Central Council for Research in Homeopathy at its various Institutes and Units throughout India during October 2005 - September 2008. A total of three hundred twenty-seven children in the age-group 6 months to 12 years were included. Trial medicines selected on the principles of homeopathy were prescribed and the diarrhea index score was assessed before and after treatment using SPSS (version 16).

Results: The difference in the mean number of stools and diarrhea index score was found to be statistically significant ($p=0.000$, <0.05) after the prescription of trial homoeopathic medicines in 321 children. The diarrhea index score got either worsened or remained unchanged from the baseline score in 6 (1.83%) children. Of the 14 medicines half of them, viz.,Podophyllum peltatum (n=158), Chamomilla (n=49), Aethusa cynapium (n=25), Mercurius solubilis (n=23), Calcarea carbonica (n=21), Sulphur (n=18), and Phosphorus (n=17) were found to be most useful among the 14 predefined trial medicines.

Conclusion: This was a:n observational study with positive results requiring further validation by suitable Randomized Control Trial(s).

Keywords: homeopathic treatment of acute diarrheal disease in children

Introduction

Acute diarrheal disease is one of the major causes of morbidity and mortality in the developing world, especially among infants and children below 5 years of age [1]. Estimates suggest that during the 1990s, nearly 1.4 billion diarrhea episodes occurred every year among children younger than 5 years of age in socio-economically developing countries, of which 123.6 million episodes required outpatient medical care and 9 million episodes required hospitalization. Approximately 2 to 2.5 million diarrhea-associated deaths were estimated annually in this age group, concentrated in the most impoverished areas of the world [2]. The percentage of children under 3 years of age who suffered from diarrhea in the two-week period before the survey was 10% in the National Family Health Survey (NFHS)-1 and 19% in NFHS-2 [3, 4]. In estimations of the burden of diarrheal diseases in India by the National Institute of Cholera and Enteric Diseases

(NICED), Kolkata indicates that diarrheal diseases contribute to about 9.1% of deaths in the age group of 0-6 years. It has been further estimated that in India the years of life lost (YLL) due to diarrheal diseases in the 0-6 years population presently contribute to about 98% of disability adjusted life-years (DALYs) and would probably remain unchanged over the next decade till 2016 [5]. For children under 5 years of age in developing areas and countries, there was a median of 3.2 episodes of diarrhea per child-year [6]. This indicated little change from previously described incidences. There has not been a concurrent decrease in morbidity rates attributable to diarrhea. As population growth is focused in the poorest areas, the total morbidity component of the disease burden is greater than previously [6].

The homeopathic system of therapy, an outcome of experimental research, is based on the principle of "Similia Similibus Curantur,"which implies that a drug cures in the sick what it causes in the healthy. According to World Health Organization, homeopathy is the second most used health care system in the world [7]. It has shown its effectiveness in treating both acute as well as chronic illnesses [8]. Homeopathy helped in controlling a cholera epidemic [9] where the mortality rate was 8.5% in comparison to 51.5% in the allopathic treatment group. Three randomized clinical trials [RCT] and one meta-analysis of these trials of homeopathic medicines on acute childhood diarrhea by Jacobs, *et al* [10-13], proved to be statistically significant in comparison to the placebo group.

In homeopathy, the treatment being person-specific and not disease-specific, there is invariably more than one useful medicine for any disease condition. As such, the feasibility of RCTs in homeopathy presents many difficulties. Moreover, before conducting an RCT we need to know about the population intended for study. No data regarding the pediatric population suffering from acute diarrhea seeking homeopathic treatment in India are available. So the present observational study of acute diarrheal diseases in children was undertaken with 14 predefined trial medicines to arrive at a group of efficacious homeopathic medicines for the treatment of acute childhood diarrhea.

Objectives

Primary objective

To evolve a group of efficacious homoeopathic medicines in the management of acute diarrheal disease in children.

Secondary objectives

i. To verify characteristic symptoms of medicines used.
ii. To ascertain clinical symptoms, if any, in respect to homeopathic medicines used during the study.

Methods

Study design

The study was a prospective, multi-centre observational study conducted at various Institutes/ Units: Central Research Institute (CRI), Noida (Uttar Pradesh), Homeopathic Drug Research Institute (HDRI), Lucknow (Uttar Pradesh), Drug Proving Research Unit (DPRU), Kolkata (West Bengal) and Drug Standardization Unit (DSU), extension centre, Hyderabad (Andhra Pradesh), under Central Council for Research in Homeopathy (henceforth Council) during the period October 2005–September 2008. A diarrhea index score (S1) was designed to assess the severity of the illness (Table 1). A second score (S2) from 1-7 was designed by the Council relative to duration of illness, thus a child reporting for treatment on the first day of infection was given the highest score of 7 and one reporting with seven days of infection, the lowest score, 1. The study protocol was in accordance with the Helsinki declaration [14] on human experimentation. Necessary ethical clearance was obtained from Council's Ethical Committee.

Patient population

Four hundred and sixty-nine children, between 6 months and 12 years of age, with 3 unformed stools for at least 2 consecutive days, were eligible to participate. Each child was followed up to recovery or for a maximum of 7 days. Children reporting with diarrhea of prolonged duration of more than 7 days, symptoms suggesting cholera, associated high grade fever, pseudo-diarrhea or frequent passage of small volumes of stool of normal consistency, fecal incontinence (for reasons other than diarrhea), parasitic/protozoa infestations, salmonella organisms causing gastroenteritis, persistent diarrhea, children on any other medicine for diarrhea, and those with bloody stools were excluded. Diarrhea with moderate and severe dehydration as per WHO guidelines was also excluded [15].

Selection of medicine

The selection of trial medicines was done by repertorizing the nosological symptoms [16] of acute diarrhea. Tyler and Weir's elimination method [17] of repertorization was used for the selection of trial medicines. "Diarrhea in Children" was taken as the eliminating rubric and thus 14 medicines of 3 marks (first grade) were short-listed using *The Complete Repertory* in Cara professional software [18]. These medicines were *Aethusa cynapium, Calcarea sulphurica., Calcarea carbonica, Chamomilla, Magnesia muriatica, Mercurius solubilis, Psorinum, Ipecacuanha, Rheum palmatum , Silicea, Stramonium, Sulphur, Phosphorus* and *Podophyllum peltatum.* These medicines were procured from M/s Sharda Boiron Laboratory Pvt. Ltd., Sahibabad, India. Each child received a homeopathic

medicine selected on the basis of presenting totality . However, if the choice of medicine was outside of the trial medicines then that child was not enrolled and was instead treated in the general out-patient department.

Potency, doses & repetition

All the enrolled patients were given medicine in 6C (10^{-12} dilution) potency in frequent doses (2-6 hourly) depending upon frequency, duration and intensity of the symptoms. Each dose consisted of 4 globules, size no. 30. After the first prescription, if improvement stalled, the next higher potency; i.e., 30C, was given. Placebo globules were given as soon as the improvement was observed.

Treatment plan

Homeopathic treatment was given as per instructions given in Hahnemann' s *Organon of Medicine* [19]. Its characteristics are: Selection of one drug at a time, using the 'similia principle'– the drug picture and disease picture should be as similar as possible. Investigators were allowed to change the prescription up to three times from among the trial medicines if the first prescription didn't work [DEFINITION OF WORK?]. As a part of non-medical management all the guardians/parents were advised to make their child take oral rehydration therapy (ORS), if necessary.

Outcome assessment

A diarrhea index score was used to quantify the severity of illness as mentioned in the study design. The diarrhea index score (S1) was divided according to intensity of the disease into mild (2-7), moderate (8-18) and severe (19-26). Assessment was done by calculating the percentage using the formula [(S1 at baseline–S1 at completion of the study) /S1 at baseline]. Thus 100% was defined as cure , >75% -<100% as marked, 50% - <75% as moderate, 25% - < 50% as mild, < 25% as insignificant improvement, 0% as not improved or status quo, and any increase in symptom score from the baseline score was counted as worse.

Statistical analysis

Descriptive statistical characteristics and comparative analyses like t test and one-way Anova was done using *SPSS* (Statistical package for social science) *Version 16*. A linear regression model was used to adjust for disparities in patient characteristics at the initial visit.

Results

During the two-year eleven-month period, 469 children were enrolled by different Institutes/Units under the Council, out of which 25 were lost to follow up, 14 were withdrawn, 103 were excluded due to their enrolment on the first and second days of illness; however, these children were followed up and the data were analyzed separately. A total of 327 children (194 males; 133 females), as per the inclusion and exclusion criteria, were followed up and studied [Mean age of children less than one year was 10.1±.2.9 months; for children above one year mean age was 5.6±3.2 years]. The incidence of acute diarrhea was mostly in the 1-5 years of age group (n=155) followed by the 6-10 years age group (n= 125), followed by those less than one year (n=47). Descriptive characteristics of children at baseline are given in Tables 2 and 3.

The S1 was evaluated at baseline and at end of the study using paired t test (Table 4). The difference in the mean S1 was found to be statistically significant (P= 0.000, <0.05). A paired t test for the average number of stools per day for all children indicated a statistically significant difference between baseline and at the end of the treatment (t=44.2, df =326, P= 0.000, <0.05).

A linear regression model containing the variables age, sex, diarrhea-index score, and number of stools in the past 48 hours was used (because age, diarrhea index score, and number of stools were found to be highly correlated; only the variable age was used in the model as an independent factor, with number of stools at the end as the dependent factor). The result of this analysis is statistically significant (p =0.000, <0.05).

An analysis of the trial medicines (Table 5) showed that 7 of the trial medicines were prescribed frequently to the children (n= 312, 95.1%) suffering from acute diarrhea; they were: *Podophyllum peltatum* (n= 158; 48.3%), *Chamomilla* (n=49, 15%), *Aethusa cynapium* (n=25;7.6%), *Calcarea carbonica* (n=21,6.4%), *Mercurius solubilis* (n=23, 7%), *Sulphur* (n=18, 5.5%), and *Phosphorus* (n=17,5.2%). Among the trial medicines 4.9% (n=6) used less often in this study were: *Ipecacuanha* (n=7), *Magnesia muriatica* (n= 2), *Psorinum* (n=2), *Rheum palmatum* (n=2), *Silicea* (n=2), and *Calcarea sulphurica* (n=1). The characteristic indications of the medicines found useful in 10 or more children are described in Table 6.

Data of children who were enrolled within 48 hours of suffering from diarrhea are as follows: 103 (59 males; 44 females). [Mean age of children less than 1 year was 9.6±.2.2 months; children above 1 year were 4.7 ±3 years.] The mean number of stools of these children at entry and at end was 7.2±2.7 and 0.1±1.1 respectively. Paired t test was done related to the diarrhea index score and the results were found to be statistically significant (p=0.000, <0.05).

One way ANOVA was carried out for all the children (n=431), making three groups according to days of infection (1st – 2nd 3rd, and 4th -5th day of illness) and their improvement status respectively . It was found that children belonging to the 1 st-2nd day of infection group responded more in comparison to the other two groups; F (2, 429)=8.64, p=0.000 <0.05.

93.2% of children (n=305) were cured at various days of their treatment (Figure 1). Most of the children (n=109) were cured on second day of their treatment. Only 10 children had showed marked degree of improvement and 4 children mild improvement, while 4 children suffered worsening of their diarrhea and were referred for other treatment, and 2 children remained status quo.

Discussion

The present study reflects the positive results of homeopathic therapy in children suffering from acute diarrhea. This study also supports the findings of the previous studies [10-12] that individualized homeopathic treatment decreases the duration of diarrhea and number of stools in children with acute diarrhea.

However, there was no data regarding the pediatric population suffering from acute diarrhea coming for homeopathic treatment in India. Moreover, India is a country otherwise known as a sub-continent with diverse geographical, cultural and dietary variations. This was the reason we elected to conduct this observational study, although RCTs [10-12] have been conducted in the past outside India, though in limited populations.

Children with diarrhea of 3-7 days' duration were enrolled; some of whom might well have been on the verge of a natural recovery. However most of the patients (80.8%) enrolled on the third day of their illness and only a few (2.4%) were enrolled on fifth day of illness. Moreover, according to Strina, *et. al.* [20], acute diarrhea may persist as long as 8-13 days, and 4% of children fall in this category. So bias due to natural regression of disease might be negligible.

In this study we observed that the mean number of stool at entry and at end was 7.2±2.7 and 0.2±1.1 respectively. The result showed a statistically significant decrease in the number of stools (p=0.000) and thus was similar to the findings of Jacob [10-12] (7.9±3.6 at baseline) [11]. Similarly the mean days of suffering from diarrhea in our study was found to be 3.2±0.4 and the days required for the diarrhea index score to become zero was 3.2±1.5, which further corroborates with findings of Jacob, *et. al.* [11]. But the difference is that in this study we enrolled children after two consecutive days of unformed stool while the later enrolled the children with 3 unformed stools within 24 hours. On considering all the cases (n=430), it was observed that the mean days of suffering from diarrhea at entry was 2.9±0.6 and the mean days for the diarrhea index score to become zero was 3.5±1.5, which is less than Jacob's [12] findings (3.6±1.9).

Similar to previous studies, [11, 12] male children were more affected than female children. This study was conducted both in urban and suburban areas. Though the children were advised to report daily until the seventh day of illness, this couldn't be achieved because, as soon as the children began to improve, the parents reported irregularly. So data for all the days of treatment was not available though the final recovery was reported.

The trial medicines useful in this observational study were *Podophyllum, Chamomilla, Mercurius solubilis, Aethusa cynapium, Phospohorus* and *Calcarea carbonica,* which are similar to the medicines used by Jacobs, *et. al.,* [12] but *Arsenicum album* was found useful in the latter study whereas it was not used in our study because it appears in the second degree in the repertory.[18]

Stool of all the children at the screening level were examined for protozoa and parasites, and, if found, these patients were excluded. Stool culture was not done to ascertain microbiological causes of diarrhea. However in one patient the cyst for *Entamoeba histolytica* was found when the stool was re-examined when the child worsened; there was no evidence of this infection at enrollment time. Such data compromises the analysis of the effect of homeopathic medicines on pathogens causing diarrhea, somewhat limiting the reliability of this study.

The strength of this study is that it provides a pragmatic representation of homeopathic practice, reflecting day-to-day clinical practice. Discovery of new clinical symptom(s) (symptoms not already present in the Materia Medica) of the trial medicines was another objective of the study; however, from analysis of the symptoms of relieved patients, no new clinical symptoms were noticed.

As the study did not have any control group, randomization or blinding, we can't conclude, based upon these findings, that homeopathic therapy is effective in acute diarrhea prevalent among the children of India. To validate the effect of homeopathic care on acute diarrhea further research is warranted in the same population. This subject–the efficacy of homeopathy for diarrhea of a specific etiology–should be studied in a more thorough manner in the future.

Conclusion

This was an observational study with positive results and these results need further validation by suitable Randomized Control Trials.

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Conflict of interest

We declare no conflict of interest.

Symptom/signs	Score				
	0	1	2	3	4
No. of Stools / day	Normal	4	6	8	12
Diarrhea (consistency)	Normal stool	Loose	Watery	Slimy	Mucus
Fever	Absent		Low grade		High grade
Vomiting / day	Absent	Only once	2 – 3	3 – 5	
Gross/Occult blood in stool	Absent			Fresh blood	Black
Weakness	Absent	Mild	More		Profound has to rest
Muscular cramps	Absent	Mild	Moderate	Severe	
Weight loss	None			< 5%	Mild (5-6%)

Table 1: Diarrhea index score

Symptom/signs	Score				
	0	1	2	3	4
No. of Stools / day	Normal	4	6	8	12
Diarrhea (consistency)	Normal stool	Loose	Watery	Slimy	Mucus
Fever	Absent		Low grade		High grade
Vomiting / day	Absent	Only once	2 – 3	3 – 5	
Gross/Occult blood in stool	Absent			Fresh blood	Black
Weakness	Absent	Mild	More		Profound has to rest
Muscular cramps	Absent	Mild	Moderate	Severe	
Weight loss	None			< 5%	Mild (5-6%)

Table 2: Baseline details of children suffering from acute diarrhea

Symptoms/signs (n)	At baseline			At end		
	No. of children	Percentage (%)	Total %	No. of children	Percentage (%)	Total %
No. of stools per day 4/6/8/12	69/125/68/65	20.8/38.2/21.1/19.9	100	6/2/2/1	1.8/0.6/0.6/0.3	3.3
Diarrhea (consistency) Loose / watery/ slimy / mucoid	51/248/26/2	15.6/75.8/8/0.6	100	9/5/2/1	2.7/1.5/0.6/0.3	5
Fever Low grade/high grade	144/1	43.9/0.3	44.2	7/1	2.1/0.3	0
Vomiting / day Only once/2-3 times/3-5 times	73/59/16	22.3/18/4.9	45.2	3/2/1	0.9/0.6/0.3	1.8
Weakness Mild/ more/ profound has to rest	92/26/5	28.1/8/1.5	37.6	¼/2	0.3/1.2/0.6	2.1
Muscular cramps Mild	4	1.2	1.2	4	1.2	1.2
Weight loss (dehydration) Less than 5%	9	2.7	49.7	9	2.7	2.7

Table 3: Presenting symptoms / signs of acute diarrhea in children

	Mean score at entry ± SD (n)	Mean score at end ± SD (n)	95% confidence interval level
Diarrhea index score	6.5±2.2 (327)	0.3±1.7 (327)*	5.94-6.52
Range in diarrhea index score			
Mild (2-7)	5.3±1.3 (218)	0.2±1.3 (218)*	4.75-5.26
Moderate (8-18)	9.2±1.3 (109)	0.5±2.1 (109)*	8.27-9.11
No. of stools per day	7.2±2.7 (327)	0.2±1.1 (327)*	6.68-7.30

Table 4: Diarrhea index score at entry and at end

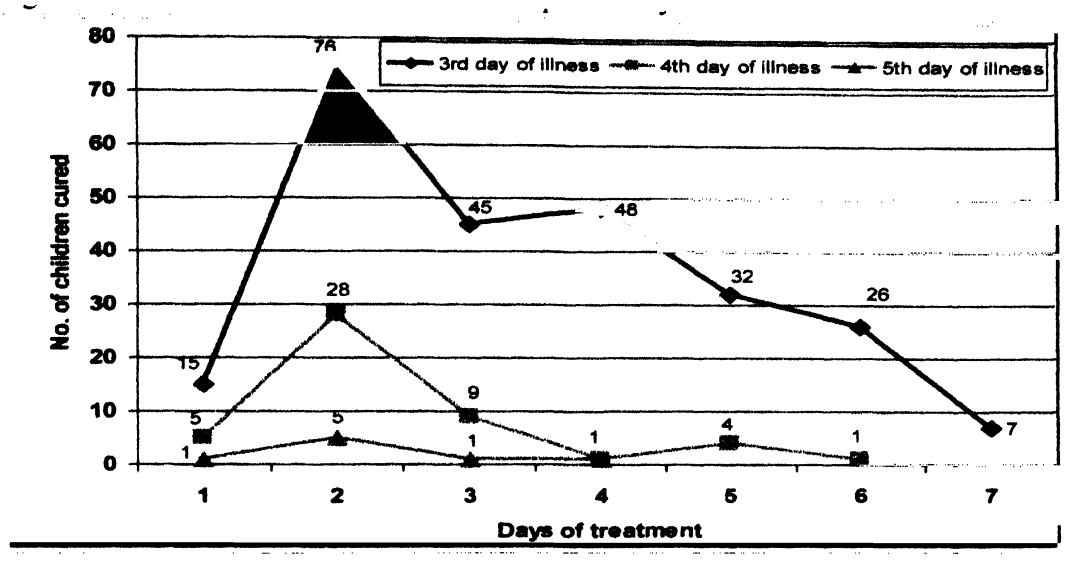

Figure 1: Number of children cured relative to the day of illness they were treated

Medicine	*No. of patients*	*Percent*	*p-value*	*95% confidence interval difference*	*Outcome assessment*[1]					
					Cured	*Marked >*	*Moderate >*	*Mild >*	*<*	*=*
Podophyllum	158	48.3	0.000	5.65-6.46	149	7	1	0	1	0
Chamomilla	49	15	0.000	6.08-7.38	48	0	1	0	0	0
Aethusa cynapium	25	7.6	0.000	5.98-8.73	22	0	1	1	1	0
Mercurius solubilis	23	7	0.000	5.12-7.48	20	1	1	0	1	0
Calcarea carbonica	21	6.4	0.000	3.95-6.62	20	0	0	0	1	0
Sulphur	18	5.5	0.000	5.11-7.22	18	0	0	0	0	0
Phosphorus	17	5.2	0.000	5.21-7.84	16	1	0	0	0	0
Ipecacuanha	7	2.1	0.000	4.55-9.44	7	0	0	0	0	0
Magnesium muriaticum	2	0.6			0	0	0	0	0	2
Psorinum	2	0.6	0. 042	1.14-13.85	1	1	0	0	0	0
Rheum	2	0.6	0.182*	-23.36-40.26	2	0	0	0	0	0
Silicea	2	0.6	0.126*	-3.85-8.85	1	0	0	1	0	0
Calcarea sulphurica	1	0.3	0.000		1	0	0	0	0	0
Stramonium	0	0	0	0	0	0	0	0	0	0
Total	327				305	10	4	2	4	2

**Not significant, p=> 0.05; [1]>- Improvement; < worse; = status quo*

Table 5: Data of trial medicines in the study

Name of trial medicine	*Indications*
Podophyllum peltatum	Diarrhea painless, putrid, with prostration, < hot weather, < morning; stool profuse, forcible with noise; profuse thirst. Color of stool changes with each stool.
Chamomilla	Irritable, wants to be carried, cries during sleep. Stool is watery, greenish; very offensive, smells like rotten eggs, <evening, night. Thirsty, drinks eagerly. Dentitional diarrhea.
Aethusa cynapium	Complete absence of thirst; weakness & prostration. Milk intolerance, can't digest milk/ intolerance to milk. Sleepiness after each stool. Diarrhea during dentition.
Calcarea carbonica	Slow in activities; fatty and flabby children, profuse sweating esp. from head; obstinate. Sour smelling stool, white chalky stool. Milk intolerance.
Mercurius solubilis	Hyperactive, destructive, disobedient. Profuse thirst with moist tongue. Slimy, offensive stool, excoriation around anus, tenesmus before and after stool, < night. Profuse sweating, too offensive.
Phosphorus	Chilly patient; lean, thin, affectionate child. Longs for cold drinks. Stool contains sago-like particles; great weakness and prostration. Vomiting <after drinking,
Sulphur	Craving for sweet; aversion to bath. Anal orifice red; empty sensation in stomach; early morning diarrhea, stool contains undigested food; burning sensation in anus. Diarrhea associated with skin eruptions.

Table 6: Characteristic indications of frequently used medicines

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