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Treatment of Acute Childhood Diarrhea With Homeopathic Medicine: A Randomized Clinical Trial in Nicaragua

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ABSTRACT. *Objective.* **Acute diarrhea is the leading cause of pediatric morbidity and mortality worldwide. Oral rehydration treatment can prevent death from dehydration, but does not reduce the duration of individual episodes. Homeopathic treatment for acute diarrhea is used in many parts of the world. This study was performed to determine whether homeopathy is useful in the treatment of acute childhood diarrhea.**

Methodology. **A randomized double-blind clinical trial comparing homeopathic medicine with placebo in the treatment of acute childhood diarrhea was conducted in León, Nicaragua, in July 1991. Eighty-one children aged 6 months to 5 years of age were included in the study. An individualized homeopathic medicine was prescribed for each child and daily follow-up was performed for 5 days. Standard treatment with oral rehydration treatment was also given.**

Results. **The treatment group had a statistically significant ($P < .05$) decrease in duration of diarrhea, defined as the number of days until there were less than three unformed stools daily for 2 consecutive days. There was also a significant difference ($P < .05$) in the number of stools per day between the two groups after 72 hours of treatment.**

Conclusions. **The statistically significant decrease in the duration of diarrhea in the treatment group suggests that homeopathic treatment might be useful in acute childhood diarrhea. Further study of this treatment deserves consideration.** *Pediatrics* **1994;93:719–725;** ***diarrhea, diarrhea, infantile; homeopathy, Nicaragua.***

ABBREVIATION. ORT, oral rehydration treatment.

Alternative medicine is controversial within the scientific community. It is used widely by the general population, yet few scientifically rigorous studies have been published demonstrating its efficacy. A recent survey published in the *New England Journal of Medicine* found that >30% of the US population had used alternative medical practices in 1990 to treat serious medical conditions and that 10% had visited practitioners of alternative medicine.[1] The lack of research in this area prompted Congress, in 1992, to establish the Office of Alternative Medicine within the National Institutes of Health to investigate various alternative medical practices (*New York Times*. January 10, 1993:1).

Homeopathy is a type of alternative medicine that is practiced extensively worldwide, especially in Europe, Latin America, and Asia.[2–4] In the United States, it has been estimated that 1% of the population used homeopathy in 1990.[1] Homeopathic theory is based on the premise whereby a substance that can cause certain symptoms when given in large doses to a healthy person is said to cure those same symptoms when given in very small doses to someone who is sick.

Homeopathic treatment is individualized, whereby two or more people with the same diagnosis may be given different medicines, depending on the specific symptoms of illness in each person. For example, a patient with acute diarrhea may be prescribed one of six or seven common remedies for this illness, based on the appearance and odor of the stool, whether or not there is abdominal pain or vomiting, what time of day the diarrhea is worse, the emotional state of the patient, and such general symptoms as body temperature, degree of thirst, and appetite.

There has been much debate about the efficacy of homeopathy since its inception in Germany in the late 18th century. Homeopathic medicines, made from plant, animal, and mineral substances, are diluted in a water/alcohol solution to extremely small concentrations. This dilution of homeopathic medicines to infinitessimal doses has led many scientists to reject homeopathic theory (*Consumer Reports*. March 1994: 201–206).[5] Currently, there is no scientific explanation for the mechanism of action of homeopathic medicines, although several hypotheses exist.[6,7]

Recent clinical trials in Europe have suggested a positive treatment association when homeopathic medicines are compared with placebo in the treatment of allergic rhinitis,[8] fibrositis,[9] and influenza,[10] whereas an earlier study showed no apparent treatment effect in rheumatoid arthritis.[11] In 1991, the *British Medical Journal* published a meta-analysis of homeopathic clinical trials which found that 15 of 22 well-designed studies showed positive results. The authors concluded that more methodologically rigorous trials should be performed to address the question of efficacy of homeopathic treatment.[12]

Acute diarrhea is the leading cause of pediatric morbidity and mortality worldwide. In the developing world, there are an estimated 1.3 billion episodes

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of diarrhea and 5 million deaths each year from this illness in children less than age 5.[13–15] In Nicaragua, diarrhea is the primary cause of mortality during the first year of life and constitutes 19% of all outpatient consultations in children 1 to 4 years old.[16]

Oral rehydration therapy (ORT), which includes the administration of oral rehydration solution along with continued feeding, is the currently recommended treatment for acute childhood diarrhea in the developing world.[17] Although this treatment is effective in preventing death from dehydration, it does not decrease the amount of diarrhea nor does it shorten the duration of individual diarrheal episodes.[18,19] Antimicrobials are not recommended in most cases of childhood diarrhea,[14,20] although inappropriate use of antibiotics for this illness is widespread in the developing world.[21,22]

Although the homeopathic literature contains numerous anecdotal reports of successful treatment of diarrhea with homeopathic medicines,[23–25] these claims have never been subjected to a formal clinical trial. Acute childhood diarrhea was thought to be an ideal condition for a homeopathic trial for several reasons: (a) the short duration of illness would allow for intensive follow-up; (b) there is no standard allopathic treatment that would have to be withheld during the trial; and (c) the public health importance of this illness is great. A pilot study of 33 cases of childhood diarrhea treated with homeopathy versus placebo was conducted in Nicaragua in the summer of 1990.[26] The results were not conclusive, due to the small sample size, but did show a signficant difference in the number of stools on the third day of treatment.

If homeopathy were shown to be effective in reducing the duration of acute childhood diarrhea, it could have a positive effect on pediatric morbidity and mortality in the developing world. Information about the clinical efficacy of homeopathic treatment in such a trial could also add to the paucity of published research in this area of alternative medicine.

METHODS

A placebo-controlled double-blind clinical trial of homeopathic treatment for acute childhood diarrhea was conducted in two municipal health clinics in León, Nicaragua, from June 25 through July 19, 1991. These clinics, located in the poor neighborhoods of Subtiava and Recreo, are each staffed by a government-paid primary care physician. Each provides free health care to the surrounding population. Children with mild to moderate diarrhea are treated in these clinics, whereas those with severe dehydration are transferred immediately to the hospital.

All children aged 6 months to 5 years who were brought to the clinics during this period with a history of acute diarrhea, defined as the passage of three or more unformed stools during the previous 24 hours, were considered for enrollment in the study. Children with a history of diarrhea for more than 1 week were excluded from the study, as well as those who had received more than one dose of an antibiotic, antiparasitic, or antispasmodic medication within the 48 hours before entry into the study.

There were no homeopathic practitioners in the city of León, so it was not expected that any of the children would have had prior homeopathic treatment. Informed consent was obtained from the parent or guardian using a disclosure statement that had been approved by the Human Subjects Review Committee of the University of Washington.

An initial history was taken, a physical examination was completed, and a stool specimen was obtained. Length and weight were measured using an infant/child height measuring board (Shorr Productions, Silver Spring, MD) and a hanging spring-dial scale (CMS, Inc, London, England). All laboratory tests were conducted by a trained laboratory technician at the León Municipal Hospital. Bacterial culture was performed for enteropathogenic organisms using McConkey's and SS (Salmonella/Shigella) agar. Suspected colonies of *Salmonella, Shigella,* and *Escherichia coli* were verified by conventional biochemical tests and serologically subtyped using slide and tube agglutination. Techniques for detection of *E coli* enterotoxins were not available in León. Examination for ova and parasites using both saline and Lugol's solution was conducted. Rotavirus assays were performed using latex fixation (MERITEC, Meridian Diagnostics, Cincinnati), and/or an Elisa test (IDEIA, Celltech Diagnostics, Cambridge, UK).

Patients were assessed for dehydration by study personnel based on a standardized World Health Organization scheme of signs and symptoms.[27] Type A dehydration is characterized by no symptoms of dehydration. Type B dehydration is diagnosed when two or more of the following signs and symptoms are present: greater than normal thirst, small amount or dark urine, child sleepy or irritable, tears absent, sunken eyes, dry mouth and tongue, faster than normal respiration or pulse, sunken fontanelle, and poor skin turgor. Type C dehydration is defined by the presence of two or more of the following: unable to drink, no urine for 6 hours, child very sleepy, unconscious, floppy, or having seizures, no tears, eyes very dry and sunken, mouth and tongue very dry, very fast or deep respiration, pulse very fast, weak, or imperceptible, fontenelle very sunken, very poor skin turgor.

Children with type C dehydration were transferred immediately to the hospital for intravenous therapy and were not included in the study. For types A and B, ORT was prescribed according to standard World Health Organization protocols.[27] Parents were advised to continue the child's normal diet, as well as breast-feeding when applicable.

A diarrhea index score was assigned to each child at the initial visit as an indicator of the severity of illness. This previously described index[28] was modified for children to include the degree of dehydration. Vomiting was assessed as none, some, or frequent, with corresponding scores of 0, 1, and 2, respectively. Abdominal pain, as reported by the mother, was scored as none (0), some (1), and much (2). Temperature was scored as follows: <37.25°C (0), 37.25 to 38.25°C (1), 38.35 to 39.35°C (2), and >39.35°C (3). The number of unformed stools in the previous 24 hours were scored as: none (0), one (1), two to three (2), four to five (3), six to seven (4), eight to nine (5), and ten or more (6). Dehydration was included as type A (0), type B (1), and type C (2).

A homeopathic interview and examination of each child was conducted by an experienced homeopathic practitioner from the United States, including two of the authors (JJ, DC). Information about the nature of the stools, abdominal pain and/or vomiting, the mood and temperament of the child, degree of thirst and appetite, presence of a fever, abdominal bloating, sleep disturbance, amount of perspiration, and other characteristic signs and symptoms was collected and entered into a computerized homeopathic expert system (RADAR, Archimed, Inc, Namur, Belgium). The results of the computer analysis were used to prescribe an individualized homeopathic medicine for each child. Indications for some of the most common homeopathic remedies for acute diarrhea can be seen in Table 1.[24,29] Only one homeopathic medication was prescribed for each child for the duration of the study.

Homeopathic medications that are commonly used for acute diarrhea were available to the homeopathic practitioners at the study location. For each of these medications, there was a box of tubes in sequentially numbered order which had been previously randomized into treatment or control medication using a random numbers table in blocks of four. These medications were prepared in the United States by a homeopathic pharmacist by impregnating pellets made of 85% sucrose and 15% lactose with a liquid homeopathic dilution in the 30C potency (the active substance was diluted 1:100 in a water/alcohol solution 30 times for a final concentration of 1×10^{-60}).

Identical pellets without homeopathic medication were used for placebo. There was no detectable difference in taste, odor, or color between the treatment medication and placebo, and they were packaged in identical blue plastic tubes that were sealed at the laboratory and remained unopened until delivery to the patient. When a homeopathic prescription was made, the next tube in order was taken from the appropriate box for that medicine and

TABLE 1. Common Homeopathic Remedies for Acute Diarrhea and Their Indications for Use[24,25]*

Arsenicum album (arsenic trioxide)
- Mind: **Great anxiety and restlessness.** Tossing about in bed. Fearful, doesn't want to be alone.
- General: Prostration. **Worse after midnight.** Burning heat with thirst for small amounts. Chilly, better being covered, cold sweats. Vomiting immediately after eating or drinking.
- Stools: **Acrid, burning, excoriating.** Diarrhea worse at night, after midnight. Putrid, bloody, odor of rotten eggs.

Chamomilla (German chamomile)
- Mind: Capricious; irritable; quarrelsome, nothing pleases. **Asks for something, then rejects it,** striking out, sensitive to pain; moaning; frenzied. **Better being carried.**
- General: One cheek red, other pale; hot; worse from heat, better from cold drinks; worse evening, until midnight.
- Stools: Green, slimy, offensive, like chopped grass. **Diarrhea during teething.** Smelling like rotten eggs; colic with diarrhea, better after stool.

Mercurius vivus (quicksilver, metallic mercury)
- Mind: Slow, lethargic, weakness of memory.
- General: **Chills alternating with heat, profuse perspiration.** Worse in evening and night. **Profuse salivation,** offensive breath, indented tongue. Violent thirst for cold drinks. Abdominal colic, better lying.
- Stools: **Slimy, scanty, lienteric, bloody.** Acrid, corrosive, frothy, yellow. Sour odor.

Podophyllum (May-apple)
- Mind: Diarrhea after mental excitement. Fidgety and restless.
- General: Gagging or empty retching. Violent cramps of the feet, calves, and thighs. Head sweats during sleep. **Thirst for large quantities of cold water.**
- Stools: **Profuse, frequent, gushing, painless, watery.** Bloody with green mucus, very offensive. **Rectal prolapse.** Exhaustion after stool. Diarrhea during teething, after fruit.

Sulphur (flowers of sulphur)
- Mind: Irritable, indifferent, weeping
- General: Cold sweat on face and feet. Blue circles under eyes, weakness. Thirsty for cold drinks, little appetite.
- Stool: Diarrhea worse at night, after milk; involuntary, sudden expulsion. **Worse 5:00 AM. Red ring around anus.** Offensive, acrid stools. Painless; sour; thin; watery. **Odor of rotten eggs.**

* **Bold type** indicates the most important symptoms for each medicine.

given to the patient. As such, both patient and providers were blind as to the treatment group.

Parents were instructed to give the child one pellet of medication orally after each unformed stool and were given a simple card with easy-to-follow diagrams to record the type and time of each stool for the next 24 hours. Follow-up home visits were made daily for the next 5 days by community health workers, who reviewed the information about stools from the card with the parent, ascertained any additional symptoms, examined the child for dehydration, and left another card for recording of stools by the parent for the next 24 hours. Any child whose condition worsened, either by a change in dehydration status or by an increased number of stools, was to be referred back to the clinic for further treatment. At the end of 5 days, each child was reweighed.

Because of the time delay in receiving laboratory results, children with parasites in the stool were not identified until after the end of the treatment period in most cases. Standard antiparasitic medications were prescribed at the end of the 5-day treatment period for children found to have parasites in the stool.

The duration of diarrhea was defined as the number of days after entry into the study until there were less than three unformed stools per day for 2 consecutive days. This definition was used in the preliminary study,[26] and was chosen before data collection as the primary outcome measure for this study. Other outcomes, including the number of days until there were 50% or fewer unformed stools than at the initial visit (a measure used by other recent diarrhea studies),[28,30] the number of days until the first formed stool, and the mean diarrhea-index score for each case over the 5-day treatment period were also examined. The average number of stools per day for each of the 5 days of treatment was compared between the two groups.

All statistical analyses were done before breaking the randomization code, using the program Epi-Info (USC, Incorporated, Stone Mountain, GA). Sample size calculations using a power of 80% and an α of .05 (two-sided test) showed that 100 children would be needed to show a 1-day difference in duration of diarrhea, which was thought by the authors to be clinically significant. Differences in descriptive characteristics at the initial visit were compared using the two-sample, two-tailed t-test for continuous data, and the χ^2 test for categorical data. The Wilcoxon rank sum test for nonparametric data was used to compare the outcome measures. A Mantel-Haenszel stratified odds ratio was used to determine whether duration of diarrhea before entry into the study was related to the response to treatment.

RESULTS

Ninety-two children initially were randomly assigned to treatment and control groups. Five cases, three from the treatment group and two controls, were mistakenly entered into the study by local personnel and were withdrawn after chart review revealed that they did not meet eligibility criteria. This occurred before any data analysis was performed or the randomization code was broken. Three of these had received more than one dose of prior antidiarrheal medication, one was less than 6 months old, and one had only two unformed stools in the 24 hours before entry into the study. Four patients were lost to follow-up because of inability to find their homes, two from the treatment group and two controls. In addition, two children were removed from the study before the end of the treatment period by their parents, who elected to give other treatment, one each from the treatment and control groups. All the remaining 81 children had complete 5-day follow-up.

A comparison of the descriptive characteristics at entry into the study of the 87 eligible children is presented in Tables 2 and 3. There were no significant differences between the treatment and control groups in the average number of unformed stools in the previous 24 hours, the duration of diarrhea before entry into the study, and the diarrhea-index score. There was no significant difference between the two groups in the proportion of children who had received prior treatment with ORT or antidiarrheal medication. Stool specimens were obtained from 74 of the eligible

TABLE 2. Comparison of Descriptive Characteristics at Initial Visit: Treatment and Control Groups (Means with Standard Deviation)

	Treatment (n = 43)	Control (n = 44)	*P* Value
Age, mo	19.6 (12.5)	17.8 (10.4)	.56
Height, cm	75.7 (8.0)	76.4 (9.0)	.70
Weight, kg	9.8 (1.9)	9.5 (2.3)	.61
Weight for height, percentile	48.5 (25.0)	42.1 (30.5)	.29
Unformed stools past 24 h	7.9 (3.6)	7.5 (3.8)	.62
Prior days of diarrhea	2.6 (1.9)	2.6 (1.5)	.87
Diarrhea-index score	5.5 (1.8)	5.6 (2.0)	.79

TABLE 3. Comparison of Descriptive Characteristics at Initial Visit, Treatment and Control Groups

	Treatment, % (n = 43)	Control, % (n = 44)	*P* Value
Currently breast-feeding	40	50	.33
Dehydration type A	74	70	.87
Prior oral rehydration treatment	9	14	.53
Prior allopathic treatment	21	11	.23
Stool analysis	(n = 37)	(n = 37)	
Escherichia coli (EPEC)	37	27	.34
Rotavirus	7	7	1.00
Parasites			
Entamoeba hystolytica	5	5	1.00
Giardia lamblia	16	22	.55
Others	11	14	.72

TABLE 4. Homeopathic Medicines Prescribed in the Treatment of Acute Childhood Diarrhea, Treatment Versus Control

Medicine	Treatment (n = 43)	Control* (n = 44)	Total (%)
Podophyllum	14	13	27 (31.0)
Chamomilla	8	5	13 (14.9)
Arsenicum album	5	6	11 (12.6)
Calcarea carbonica	5	2	7 (8.0)
Sulphur	4	2	6 (6.8)
Mercurius vivus	1	3	4 (4.6)
Pulsatilla	1	3	4 (4.6)
Phosphorus	2	1	3 (3.4)
Others†	3	9	12 (13.8)

* Controls actually received placebo designed to resemble the medicines listed.
† Two prescriptions each: China, Gambogia. One prescription each: Aethusia, Aloe, Belladonna, Bryonia, Colchicum, Croton tiglium, Dulcamara, Nux vomica.

children, with 37 in both the treatment and control groups. One or more agents considered to be pathogenic for acute childhood diarrhea were found in 59% of these specimens, including *E coli* with serotypes of 055, 086, 011, 0119, 0125, 0126, 0127, 0128, 0142, and 0114, rotavirus, *Entamoeba histolytica*, and *Giardia lamblia*. There was no *Shigella* or *Salmonella* isolated, and laboratory techniques for detecting enterotoxic *E coli* (ETEC) were not available.

Although 18 different homeopathic medicines were prescribed to children in the study, the three most common, Podophyllum, Chamomilla, and Arsenicum album were prescribed in nearly 60% of the cases (Table 4). Eighty-six percent of the cases received the eight most commonly prescribed medicines. There was no difference in compliance between the two

TABLE 5. Comparison of Outcomes of Homeopathic Treatment Versus Control in the Treatment of Acute Childhood Diarrhea

	Treatment (n = 40)	Control (n = 41)	*P**
Days to <3 unformed stools on 2 consecutive days			
Median	2.5	4.0	.048
Mean (SD)	3.0 (1.9)	3.8 (1.7)	
Days to 50% improvement			
Median	1.0	2.0	.036
Mean (SD)	1.9 (1.4)	2.7 (1.7)	
Days to first formed stool			
Median	3.0	5.5	.054
Mean (SD)	3.6 (1.9)	4.4 (1.8)	
Mean diarrhea index score			
Median	2.0	2.4	.037
Mean (SD)	2.0 (1.0)	2.7 (1.6)	
Weight/height percentile change			
Median	6.0	1.0	.30
Mean	4.6 (9.3)	2.8 (9.8)	

* Wilcoxon rank sum test used.

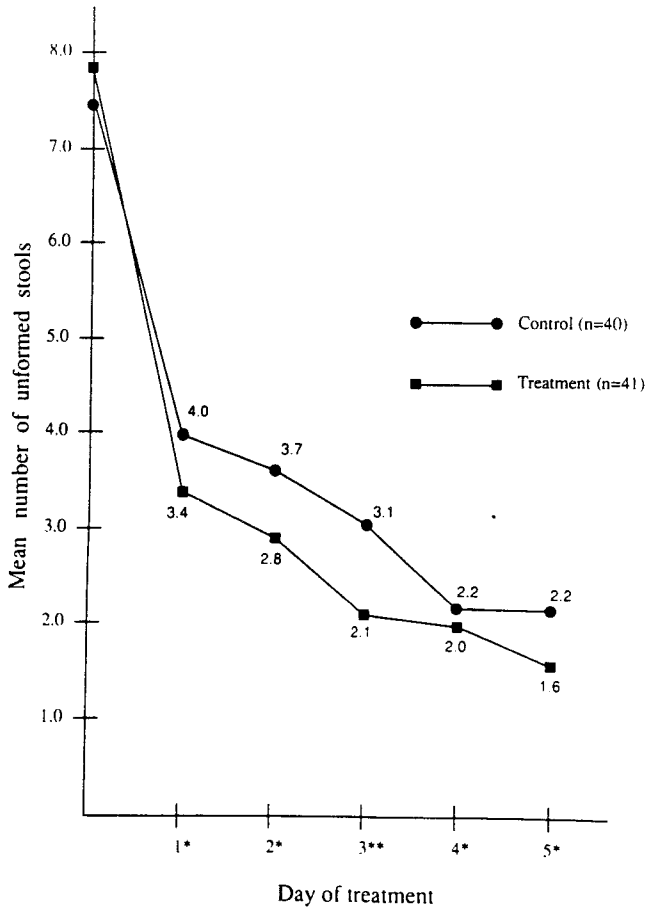

Figure. Comparison of mean number of stools by day of treatment, homeopathic treatment versus control in acute childhood diarrhea. *, NS; **, $P < .05$.

groups, as reported by the parents during the daily home visits. Eleven children were given antidiarrheal medication by their parents during the 5-day study period, six from the control group and five from the treatment group. There were no reported side effects from either the treatment or the control groups.

TABLE 6. Odds Ratios (With Confidence Intervals) of Duration of Diarrhea After Treatment (Unadjusted) Compared With Mantel-Haenszel Stratification for Days of Diarrhea Before Entry into the Study

	Active	Placebo	Odds Ratio	95% CI*
Duration after treatment (unadjusted)	n = 40	n = 41		
≤2 d	20	11		
>2 d	20	30	2.73	0.98–7.70
Days of diarrhea before entry				
Prior days = 1	n = 14	n = 13		
Duration after treatment				
≤2 d	5	4		
>2 d	9	9	1.25	0.19–8.55
Prior days >1, <5	n = 20	n = 19		
Duration after treatment				
≤2 d	13	6		
>2 d	7	16	4.33	1.01–19.6
Prior days >4	n = 5	n = 6		
Duration after treatment				
≤2 d	2	1		
>2 d	3	5	3.33	0.11–235
Mantel-Haenszel summary			2.73	0.99–8.00

* CI, confidence interval.

TABLE 7. Comparison of Outcomes by Presence or Absence of a Pathogenic Agent,* Homeopathic Treatment Versus Control in the Treatment of Acute Childhood Diarrhea (Means With Standard Deviation)

	Pathogenic Agent Present		P†	Pathogenic Agent Absent		P†
	Treatment (n = 21)	Control (n = 21)		Treatment (n = 14)	Control (n = 15)	
Days until						
<3 stools, 2 d	2.5 (1.7)	4.1 (1.8)	.006	3.8 (1.8)	3.6 (3.0)	.75
50% improvement	1.6 (1.2)	2.5 (1.5)	.034	2.4 (1.7)	2.7 (1.9)	.42
First formed stool	2.9 (1.7)	4.6 (1.6)	.003	4.6 (1.7)	4.5 (2.1)	.89
Mean diarrhea-index score	1.7 (1.0)	2.8 (1.6)	.006	2.4 (1.0)	2.8 (1.7)	.43

* Includes enteropathogenic *Escherichia coli*, rotavirus, *Entamoeba histolytica*, and *Giardia lamblia*.
† Wilcoxon rank sum test used.

The outcomes for the two groups can be seen in Table 5. The results for the primary outcome measure, number of days until there were less than three unformed stools for 2 consecutive days, as well as two of the three secondary measures showed a positive treatment association that was statistically significant at $P < .05$. It should be noted that all these outcome measures are highly correlated. There was no significant difference between the two groups in weight-for-height percentile change during the 5-day treatment period.

A graph of the mean number of stools per day for each of the two groups can be see in the Figure. The treatment group had a value on day 3 that was significantly less than that of the control group at $P < .05$. In the treatment group, the mean number of unformed stools had dropped to below three on the second day, whereas this did not occur until day 4 in the control group.

The unadjusted odds ratio for cases with a duration of diarrhea after treatment of ≤2 days compared with those with a duration of >2 days was 2.7 (0.98, 7.70) (Table 6). Stratification was carried out into three subgroups to allow for stratified analysis by duration of diarrhea before treatment; those cases in which the diarrhea had been present for 24 hours or less before treatment, cases with diarrhea for >24 hours but <5 days, and those cases with diarrhea for 5 days or more. The results of the Mantel-Haenszel stratification using these subgroups showed no change in the resulting odds ratio. The subgroup of children with diarrhea for >24 hours and <5 days were found to have the strongest association between treatment and shorter duration of diarrhea when compared with placebo. Subgroup analyses by patient compliance, physician interviewer, and homeopathic medication prescribed did not reveal any significant differences.

Although the study sample was too small for useful comparison of outcome by specific pathogens, the outcome for those cases in which a pathogenic organism was detected showed a positive treatment association that was highly significant (Table 7). This did not change when analysis was performed without *G lamblia* and *E histolytica* as pathogens, which are endemic in Nicaragua and have an unclear role as agents in acute diarrhea.[16] There was no difference in outcome between the two groups in those cases in which no pathogen was found.

DISCUSSION

No scientific explanation for the mechanism of action of homeopathy currently exists. However, the numerous anecdotal reports of its efficacy and its use by millions of people worldwide suggest the need for

a thorough scientific examination of this modality. In this study, our intention was to document whether there was a clinically and statistically significant treatment association with homeopathic treatment, not to determine mechanism of action.

These results show a statistically significant decrease in the duration of diarrhea in the group receiving treatment medication. This decrease of 0.8 days per episode may also have clinical significance, by decreasing dehydration and postdiarrheal malnutrition, as well as reducing the burden to the mother. Because the average duration of an episode of acute childhood diarrhea has been reported to be 5 or 6 days,[26,31] this 15% decrease in duration could lead to a significant reduction in morbidity. The absence of a significant difference in weight-for-height percentile change could be due to the fact that both groups received ORT, which likely prevented serious dehydration and weight loss.

The significant difference in the average number of stools per day at day 3, which confirms a similar finding in the preliminary study,[26] suggests that the usefulness of this treatment may be in the early stages of acute diarrhea. Because >80% of acute diarrheal episodes resolve spontaneously within 1 week[31] and the mean duration of diarrhea before entry into the study was 2.6 days, it is not surprising that by days 4 and 5 (which would be the sixth or seventh day of diarrhea), there was little difference in the number of stools per day between the two groups.

Because children with a history of diarrhea for up to 6 or 7 days were included in the study, it could be argued that some of these children were well on their way to recovery, regardless of any treatment that they might have received. However, stratification by duration of diarrhea before entry into the study did not change the results, which suggests that any bias from including these children was nonselective. Including these children in the study may have diminished any apparent treatment association from the medication, because both groups would have a shorter duration of diarrhea after treatment.

The finding of a stronger positive treatment association in those cases in which an etiologic agent was detected was also found in the preliminary study but should be interpreted with caution, because methods for detection of other possible pathogens, such as enterotoxigenic *E coli* were not used. Knowledge of the specific etiologic agent is not generally used by homeopaths in determining the choice of a homeopathic medicine, although this could be explored in future larger studies by subgroup analysis.

The subjective nature of the parent's report of the number of unformed stools each day could be questioned. The intensive daily home visits with review of the cards by the health workers were conducted to encourage greater accuracy in reporting by the parents. Any reporting bias would likely have occurred randomly in each of the two treatment groups and should not have affected the overall results.

An inherent methodological problem of this and any homeopathic clinical trial is the use of more than one treatment medication. Because homepathic treatment requires, by definition, individualization of the medicine to the patient, several different medicines were used in the study. Because most clinical trials evaluate the effects of a specific medicine, it is unusual for more than one medicine to be used. In this trial, it was our intent to evaluate the *system* of homeopathic treatment, rather than the specific medicines.

This study suggests that homeopathic treatment of acute diarrhea may be associated with a significant decrease in duration of diarrhea in Nicaraguan children. Because resources are scarce in developing countries, further studies in other locations should be conducted to determine whether these findings are accurate before a recommendation for homeopathic treatment of childhood diarrhea can be justified. Such studies should include larger populations that are followed up for longer periods. It would also be useful to evaluate the treatment response for individual etiologic agents, as well as to determine whether there is any effect on long-term nutritional status and recurrence rates with this treatment.

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