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Homeopathic care for the prevention of upper respiratory tract infections in children: A pragmatic, randomised, controlled trial comparing individualised homeopathic care and waiting-list controls☆

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Summary
Objective: To investigate whether individualised treatment by homeopaths is effective in preventing childhood upper respiratory tract infection (URTI).
Methods: Open, pragmatic, randomised parallel-group trial with waiting-list group as control. One hundred and sixty-nine children below the age of 10 years, recruited by post from children previously diagnosed with URTI, were randomly assigned to receive either pragmatic homeopathic care from one of five homeopaths for 12 weeks or to a waiting-list control using self-selected, conventional health care.
Result: There was a significant difference in median total symptom score in favour of homeopathic care (24 points) compared to the control group (44 points) ($p = 0.026$). The difference in the median number of days with URTI symptoms was statistically significant with 8 days in the homeopathic group and 13 days in the control group ($p = 0.006$). There was no statistical difference in the use of conventional medication or care between the two groups.
Conclusion: In this study, there was a clinically relevant effect of individualised homeopathic care in the prevention of URTI in children.
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Introduction

There are published studies on the effect of homeopathic medicine and homeopathic care for upper

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respiratory tract infection (URTI),[1] but the main body of clinical research has been in adults and has used one homeopathic medicine or a combination of several, compared to placebo; only a few studies concern the effect of individualised homeopathic care or the specific effect of homeopathic medicines for children with URTI.[2–5]

The lack of clinically relevant research in homeopathy has been emphasised.[1,6] There is a need for studies that explore pragmatically the effect of the everyday provision of homeopathic care in commonly treated conditions.

Homeopathy is frequently used for children.[7,8] In Germany, nearly a third of the patients in homeopathic medical practice are children.[9] The proportion of homeopathic consultations in Norway involving children below the age of 10 years has increased from 10% in 1985 to 26% in 1998,[10] with respiratory and skin complaints as the main diagnostic groups. Most of these children have recurrent complaints and use homeopathy as a preventative treatment. Therefore, more rigorous information about its clinical effectiveness and cost within this population group is essential in order for both health personnel and patients to make informed treatment decisions.

A Norwegian population study found that during 1 year, 4-year-old children with frequent colds and otitis media visited physicians ten times more frequently than all other children.[11] Children with upper respiratory tract infections are also frequent users of antibiotics,[12] despite some evidence of only modest clinical effect.[13]

The objective of this trial was to investigate whether individualised homeopathic care is effective in the prevention of URTI in children.

Materials and methods

Design

This was an open, pragmatic, randomised parallel-group, controlled trial, performed according to the principles of the Helsinki Declaration.[14] The regional committee for medical ethics recommended the study and it was registered with the Norwegian data inspectorate. The study was carried out in Trondheim, a city with 150,000 inhabitants in the middle of Norway.

Patients

Inclusion criteria

Children below 10 years of age who had been to a medical doctor for URTI; how often or the number of episodes were not criteria. URTI was defined as having a health problem to which the consulting doctor gave an International Classification of Primary Care code of H01 (ear pain), H71 (acute otitis media), H72 (glue ear), H74 (chronic otitis media), R72 (streptococcal infection), R74 (URTI), R75 (sinusitis) or R76 (tonsillitis).[15]

Exclusion criteria

Concomitant serious disease or daily use of medicines such as antibiotics, steroids (except in inhalators) and cytotoxic agents, and use of homeopathic medicines in the 3 months preceding inclusion.

The inclusion criteria were designed to recruit children who used the health services for their URTI and who could have an increased risk of getting an URTI in the future. The study focused on new episodes of URTI in children and recruited mainly children who had consulted the casualty department, which is part of the primary care system, at the University hospital. The trial took place in two periods to limit the study to the winter months with a high incidence of URTI: September 2002 to June 2003 and January to June 2004. The hospital database was searched for patients meeting the inclusion criteria. Patients attending the casualty department between August 2002 and January 2003 were recruited to the first period, and those attending between February and December 2003 to the second period. In addition, leaflets were distributed in November 2002 to local child health centres and an advertisement was placed in the newspaper in January 2004. Patients were sent a letter with an informed consent form included for the parents to sign and return if they agreed to participate. All patients whose parents returned the form and met the inclusion criteria were regarded as eligible, and were sent a baseline questionnaire (Fig. 1); those who returned this were entered into the study and randomised.

Randomisation

Randomisation was done by telephone/fax to an independent trial service office that provided the randomisation using a computer-generated randomisation with stratification for three age groups ($0 < 3$, $3 < 6$ and $6 < 10$ years) in blocks whose size was concealed.

Interventions

Patients randomised to homeopathic care were offered an immediate appointment with a homeopath and asked to fill in symptom diaries for 12

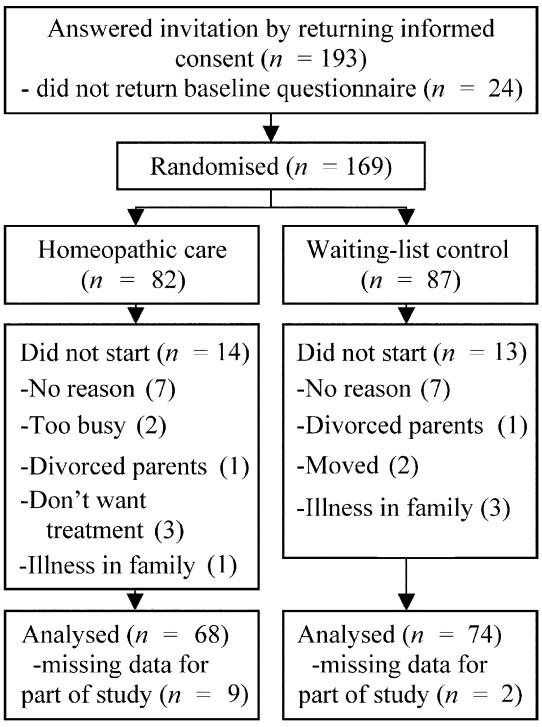

Figure 1 Flow of participants through the trial.

weeks. Patients randomised to a waiting-list group as control were told that they would get an appointment with a homeopath after having filled in the symptom diaries for 12 weeks. All participants were informed that they could use any other treatment of their own choice except any form of homeopathic medication, and that they should seek help from their general practitioner as needed.

The homeopaths were chosen from members of the Norwegian Homeopathic Association (an organisation for both medical and non-medical homeopaths). None of the homeopaths participating were medical doctors. The homeopaths had had a similar education in homeopathy and a basic training in conventional medicine. Four homeopaths were initially included, but one moved and was replaced, so five took part in the study. Three worked in a centre with other homeopaths, and two were in a sole practice. There was one man and four women; their practice experience was 2, 10, 12, 25 and 27 years, respectively.

The patients were allocated sequentially to one of the homeopaths. The homeopaths were instructed to treat the patients as they would normally, including initial and follow-up consultations. Each of the homeopaths made an independent choice of medication and could prescribe any homeopathic medicine(s) at any potency. The homeopaths sent their prescription to a homeopathic dispensary that posted the medicine(s) directly to the patients. In routine homeopathic care in Norway, the patients buy their medicine at the pharmacy, or are sent it from the pharmacy if they live in a rural area or in an area where the pharmacy does not have a stock of homeopathic medicines. The medicines were manufactured by Homeoden, Belgium according to the German Homeopathic Pharmacopoeia.[16]

To minimise interaction, the parents of the children were told that they could contact the study team if they had any questions. Otherwise, the only contact was written information sent by post.

Outcome measures

Patient diaries were used to measure outcome and were completed by the child's parents. Diaries were used to avoid the intrusive nature of assessment, to mirror real life as much as possible, and because parents can best assess their child's health.[17,18] The study lasted for 12 weeks for each of the participants; to improve compliance the participants were sent and returned diaries every fourth week.

The daily diary asked whether the child had been ill with URTI, had other illness, used antibiotics, used analgesic/antipyretic drugs, visited a medical doctor, whether someone had been absent from work due to the child's illness, and whether the child had taken the homeopathic medicines. The parents were told to 'Regard the child as ill if he/she is more ill than he/she usually is' and that an URTI was present when the child is 'ill with complaints in ear/nose/throat'. Otherwise, the parents were instructed to regard any complaint as 'other illness'. On the days when the child was ill with URTI, the parents filled in a separate symptom diary based on a score previously used by Jacobs et al.[5] for assessing the homeopathic treatment of children with otitis media. This scale also emphasises general symptoms. The difference between the score used in this study and the one used by Jacobs was that 'Other URTI symptoms' was replaced with 'discharge', 'nasal obstruction' and 'cough' (Table 1). Nine symptoms could be recorded, with a daily possible total score range of 0—11. The total symptom score was calculated by adding the scores for each day. The score is zero if the child does not have an URTI. The scale has not previously been used in a trial of URTI, so to evaluate whether it captured the general condition of the child, it was validated against a question on general wellbeing scored as normal, deteriorated or very bad on days with URTI.

The parents were also asked to score whether there were any 'noises coming from the chest' because homeopaths believe that successful treat-

Table 1 The symptom diary used by the parents when they judged their child to be ill with URTI.

Symptoms	Number of points		
	0	1	2
Fever (°C)	<38	38–39	>39
Pain	No	Complains	Screams
Mood	Normal	Bad	
Appetite	Normal	Diminished	
Energy	Normal	Diminished	
Sleep	Normal	Disturbed	
Discharge	Normal	Increased	
Obstruction, nose	Normal	Increased	
Cough	Normal	Increased	

The parents were asked to score according to how the child has been during the day. The symptoms constitute a symptom score that can reach a maximum of 11 points each day.

ment will reduce the chance of getting lower respiratory tract symptoms.[19] The homeopaths recorded every contact with the patients and the prescribed treatment.

Sample size

There were no previous data using the main outcome measure on which to base the sample size calculation, and therefore the sample size was calculated on the number of days with URTI. It was decided, in line with other rigorous pragmatic studies,[17] that the smallest difference worth detecting was a 20% reduction in number of days with URTI. It was hypothesised that non-treated children might have three episodes of URTI, each lasting 5 days, giving an expected 15 days with URTI for the waiting-list controls and 12 days for those under homeopathic care during the 12-week study period. The S.D. was estimated to be a doubling of the difference (6 days). The power calculation was done using 80% power and a 5% significance level, resulting in an estimated 63 patients per group. The aim was to recruit at least 75 patients in each group to allow for drop-out.

Analysis

Confirmatory testing of the main outcome measure was based on intention to treat, with all patients who started the study included in the analysis. There were, however, no available outcome data for those who were randomised but did not start the study (Fig. 1). The predefined primary outcome was the median total symptom score for URTI during the 12 weeks (Table 2). The secondary outcome was the median number of days with URTI symptoms. Values for the missing days for those who were lost to follow-up were replaced with the mean for the period they had participated. As the data were non-parametric they were subjected to a Mann–Whitney, two-tailed test. Pearson's χ^2-test was used for categorical data. As most data were skewed and had outliers, the distribution of the outcome measures is described with the median and the 95% confidence interval (CI) for the median. All data were analysed using *SPSS for Windows* version 12.0.1, except the calculation of the 95% CI for the

Table 2 Characteristics of children that started the study.

Characteristic	Homeopathic care ($n=68$)	Control ($n=74$)
Mean age (S.D.)	3.2 (2.2)	3.3 (2.4)
Boys (%)	45 (66.2)	39 (52.7)
Very good or good general health as judged by parents (%)	53 (77.9)	60 (81.1)
Children with frequent colds (%)	45 (66.2)	52 (70.3)
Mean number of ear infections (S.D.)	2.6 (5.3)	1.7 (2.0)
Mean number of throat infections (S.D.)	2.6 (5.2)	1.4 (1.9)
Mean number of bronchitis (S.D.)	0.9 (2.1)	0.7 (1.4)
Mean number of pneumonias (S.D.)	0.4 (1.0)	0.2 (0.5)
Had grommets inserted (%)	6 (8.8)	15 (20.3)
Had tonsillectomy (%)	4 (5.9)	7 (9.5)
Mean number of days with analgesics/antipyretics in last 3 months (S.D.)	5.3 (5.3)	4.6 (5.3)
Mean number of courses of antibiotics in last 3 months (S.D.)	0.9 (0.8)	0.6 (0.7)
Mean number of visits to medical doctor in previous 3 months (S.D.)	2.1 (1.4)	1.8 (1.6)
Non-smoking household (%)	60 (88.2)	70 (94.6)
Mean number of children in the household (S.D.)	2.1 (0.9)	2.1 (0.8)
Attending nursery or school (%)	50 (73.5)	55 (74.3)
Parents confident in homeopathy (%)	26 (38.2)	28 (37.8)

Values are either [number of children (%)] or [mean for the whole group (S.D.)].

non-normal distribution, which was done with *STATA* version 8.0.

Results

One hundred and ninety-three patients returned the informed consent and were eligible to participate. One hundred and sixty-nine of these returned the initial questionnaire and were randomised. Of these, 65 participated in the first period and 104 in the second. One hundred and thirty-four (79%) were recruited from the casualty department, 23 (14%) from the advertisement in the local newspaper and 12 (7%) from the leaflets distributed to the child's health clinics. A total of 27 (16%) patients either did not return any data (diary) or withdrew after the random allocation, leaving 74 in the waiting-list control group and 68 in the homeopathic care group (Fig. 1). The groups were comparable at baseline for demographic variables and health history (Table 2). There was no significant difference in baseline values between the groups for those who did not start the study, except for age, where those randomised to homeopathic care were older.

Eleven patients (7.7%) who started the study, nine in the homeopathic care group and two in the control, were lost to follow-up and did not return data for the whole study. Parents of two patients, both in the homeopathic care group, informed the investigator about this, stating that they were too busy to continue (self withdrawn). No one reported an adverse reaction as a reason for dropping out. Those lost to follow-up in both groups tended to have higher symptoms scores and more days with URTI than those who completed the study, although this was not statistically significant when missing values were replaced with the mean for the period they had participated.

Homeopathic care

The average number of consultations in the study period with the homeopaths was 2.9 (S.D. 0.6, range 1—4). The first consultation lasted on average 50 min (S.D. 11.8, range 30—70) and the follow-up consultations lasted 24 min (S.D. 7.8, range 10—50). Twelve (18%) patients contacted the homeopaths between the scheduled consultations and had a short telephone consultation, 10 of them once and two twice.

The homeopaths prescribed 22 different homeopathic medicines (Table 3). Calcarea carbonicum (made from oyster shell) was prescribed for nearly half of the patients at the first consultation. Nine different potencies were prescribed, with D200, C30 and D30 accounting for 75% of the prescriptions. These potencies are all well above Avogadros number ('ultramolecular') so theoretically there were no molecules of the original substance in the majority of the prescriptions.

Table 3 Homeopathic medicines prescribed at the first consultation for 68 patients, with number of prescriptions.

Remedy name[a]	No. of prescriptions at first consultation[b]
Aconitum	2
Calcarea Carbonica	32
Hepar Sulphuricum	7
Kali Muriatricum	1
Lycopodium	1
Medorrhinum	1
Mercurius Corrosivus	1
Natrum Sulphuricum	1
Opium	1
Phosphorus	3
Pulsatilla	5
Silica	8
Spongia	1
Stramonium	4
Streptococcinum	1
Sulphur	5
Tuberculinum	5
Total	79

[a] In addition, the following were homeopathic remedies prescribed during the study: Antimon Tartaricum, Belladonna, Manganum Acidum, Mercurius and Phytolacca.

[b] Eleven patients were prescribed two homeopathic medicines at the first consultation, either to use simultaneously ($n = 7$) or to use in case of acute episodes ($n = 4$).

The homeopaths did not change the first prescribed homeopathic medicine for 44 (65%) of the patients. Nineteen (28%) patients were prescribed two different medicines during the treatment, two (3%) were prescribed three different medicines and 3 (4%) were prescribed four different medicines. In total, the homeopaths changed their prescription for 18 (27%) patients during the treatment, in line with normal homeopathic treatment. The homeopaths prescribed the use of two different medicines at the same time for 12 (18%) patients, and 7 (10%) patients were prescribed a separate homeopathic medicine to use during acute episodes in addition to the medicine prescribed for prevention.

Outcome

The correlation between the total symptom score derived from the symptom diaries and general well being for all patients was highly significant, with

Table 4 Effect of treatment by homeopath ($n = 68$) compared to waiting-list controls ($n = 74$) in prevention of upper respiratory tract infection (URTI) in children.

Outcome measure	Homeopathic care median (CI)[a]	Control median (CI)[a]	P[b]
Total symptom score	24 (11.4—35.6)	44 (32.1—60.8)	$Z = 2.231$, $P = 0.026$
Days with URTI	8 (4—11.6)	13 (9.1—15)	$Z = 2.774$, $P = 0.006$
Days with antibiotic	0 (0—0)	0 (0—0)	$Z = 0.509$, $P = 0.611$
Days with analgesic/antipyretic	0 (0—1)	0 (0—1)	$Z = 0.348$, $P = 0.728$
Visits to medical doctor	0 (0—0)	0 (0—0)	$Z = 0.626$, $P = 0.531$
Days with other illness	0.5 (0—2)	0 (0—1)	$Z = 0.170$, $P = 0.865$
Days with noises from chest	0 (0—1)	0 (0—3)	$Z = 1.315$, $P = 0.189$
Days with work absence due to ill child	0 (0—0)	0 (0—1)	$Z = 1.350$, $P = 0.177$

[a] Median for whole group (95% confidence interval — CI).
[b] Mann—Whitney (non-parametric) test.

Table 5 Effect of treatment by homeopath ($n = 68$) compared to waiting-list controls ($n = 74$) in prevention of upper respiratory tract infection (URTI) in children.

Number of children who	Homeopathic care N (%)[a]	Control N (%)[a]	P[b]
Had days with URTI	54 (79.4)	69 (93.2)	$\chi^2 = 5.849$, $P = 0.016$
Had days with other illness	34 (50.0)	34 (45.9)	$\chi^2 = 0.233$, $P = 0.629$
Used antibiotics	9 (13.2)	12 (16.2)	$\chi^2 = 0.250$, $P = 0.617$
Used analgesic/antipyretic	28 (41.2)	32 (43.2)	$\chi^2 = 0.062$, $P = 0.803$
Consulted a medical doctor	19 (27.9)	26 (35.1)	$\chi^2 = 0.847$, $P = 0.357$
Had parents with work absence when ill	25 (36.8)	33 (44.6)	$\chi^2 = 0.899$, $P = 0.343$

[a] Number of children (percentage).
[b] Pearson's χ^2-test.

a correlation coefficient of 0.812 ($P < 0.001$; Spearman's rank correlation).

There was a significant difference in the predefined main outcome in favour of homeopathic care ($P = 0.026$) (Table 4). The median symptom score for the 12-week study period was 24 (95% CI: 11.4—35.6) for the homeopathic care group and 44 (CI: 32.1—60.8) for the waiting-list control group. The difference in the median number of days for which the parents judged their child to be ill with URTI symptoms was statistically significant; the homeopathic care group reported 8 days (CI: 4—11.6) and the waiting-list control 13 (CI: 9.1—15) days ($P = 0.006$).

The number of children who had one or more days with URTI symptoms was also significantly less in the homeopathic care group ($P = 0.016$) (Table 5).

There was modest use of conventional medication (antibiotics and analgesics) in both groups, with no significant difference between them (Tables 4 and 5). Visits to a medical practitioner were also equal between the two groups. There was a tendency for less absence from work (for the parent) as a consequence of a sick child in the group receiving homeopathic care. Fifteen (22.1%) patients in the homeopathic care group self-reported having an adverse effect; all were mild and transient.

Discussion

Children receiving individualised homeopathic care had clinically relevant benefits relating to the prevention of URTI over a 12-week study period.

The strength of this study is that it is pragmatic, mirroring real life for parents of children with URTI and the treatment that they can expect if they consult a homeopath. This study was developed from information obtained from everyday homeopathic practice.[10] Its methodological strengths include an adequate sample size and concealed randomisation.

As this study was a pragmatic trial, the control group received no placebo intervention or extra consultations over the study period. Patients were not blinded and therefore it is possible that they were biased in their scoring. It is not possible to account for the influence of this on the observed differences. To ensure that the homeopaths were not involved in informing the patients about the study or in handling the patients' diaries, all forms/diaries were sent by the study team directly to the participants and returned the same way. To minimise contact with the participants, it was decided not to have a recruitment meeting with the patients or to phone them during the study. This could explain the relatively large num-

ber of patients not starting the study even though they had returned both their informed consent and basic questionnaire before randomisation. As no data were available for these patients, they were not included in the analysis. An equal number in each group did not start and there were no significant differences between them. It is not possible to know what impact these would have had on the study results if they had participated.

The diaries were designed to capture the parent's judgement of the condition of the child. This was done to mirror everyday life, where parents are the ones that decide if their child is ill or not. The symptom diary used to calculate the main outcome was chosen because it captures the general condition of children during episodes of URTI (content validity), and is easy and simple for parents to complete. The construct validity of the symptom diary was tested against a question on the child's general well being and showed good correlation, indicating that it measured what it was intended to measure. The criterion validity and reliability of the symptom diary was not formally tested.

Comparison with other studies

Placebo-controlled studies of homeopathy for URTI in children have suggested a tendency, although not significant, toward a specific effect from homeopathic medicines.[4,5] An open, randomised trial found that significantly more children with glue ear progressed to a normal tympanogram after receiving pragmatic homeopathic care than those receiving standard care,[2] as well as a trend for more children with improved hearing in the homeopathic care group. A comparative, non-randomised trial of children with acute otitis media found a trend toward faster resolution of pain and fewer recurrences in children who received treatment from a homeopathic rather than conventional ear/nose/throat specialist.[3] The present study adds to the claim that there seems to be an effect from the provision of individualised homeopathic care for children with URTI. But, as this was a pragmatic study, it provides no evidence to sustain an argument that homeopathic medicines have specific efficacy.

What constitutes the effect?

Does the observed benefit relate to the effect of the homeopathic medications or to the process of the homeopathic consultation and the subsequent homeopathic prescription? It is likely that both these factors may have influenced the outcome. But as those randomised to receive homeopathic care had both extra medication and support during the study period, this study supplies no information on to what extent the process or the medication contributes to the observed effect.

Conclusion

Child patients receiving homeopathic care experienced fewer days with URTI and fewer symptoms from the URTI, indicating that the whole package of individualised homeopathic care is beneficial in the prevention and treatment of URTI in children. The increase in the proportion of children visiting homeopaths in Norway may be a result of a lay knowledge about this beneficial effect.

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