Effect of homoeopathy on pain and other events after acute trauma: placebo controlled trial with bilateral oral surgery

Per Lökken, Per Atle Straumsheim, Dag Tveiten, Per Skjelbred, Christian Fredrik Borchgrevink

Abstract

Objective—To examine whether homoeopathy has any effect on pain and other inflammatory events after surgery.

Design—Randomised double blind, placebo controlled crossover trial with "identical" oral surgical procedures performed on two separate occasions in 24 patients.

Interventions—Treatment started 3 hours after surgery with either homoeopathy or placebo.

Main outcome measures—Postoperative pain and preference for postoperative course assessed by patients on visual analogue scales. Measurements of postoperative swelling and reduction in ability to open mouth. Assessment of bleeding after surgery.

Results—Pain after surgery was essentially the same whether treated with homoeopathy or placebo. Postoperative swelling was not significantly affected by homoeopathy, but treatment tended to give less reduction in ability to open mouth. No noticeable difference was seen in postoperative bleeding, side effects, or complaints. Thirteen of the 24 patients preferred the postoperative course with placebo.

Conclusions—No positive evidence was found for efficacy of homoeopathic treatment on pain and other inflammatory events after an acute soft tissue and bone injury inflicted by a surgical intervention. Differences in the order of 30% to 40% would have been needed to show significant effects.

Introduction

The question of whether the infinitesimally diluted substances used in homoeopathy really exert biological activity is of considerable interest and importance and involves both scientific, economic, and medical aspects. A meta-analysis in the *BMJ* in 1991 of 107 controlled clinical trials of homoeopathy concluded that evidence of the efficacy of homoeopathy in humans is positive but not sufficient to draw definite conclusions.¹

The present study is part of a research programme, supported by the Norwegian Research Council, to evaluate the efficacy of various forms of alternative medicine. One author (CFB) is the coordinator of this programme, two (PAS, DT) are experienced practitioners of homoeopathy, and two (PS, PL) are well versed with the clinical surgical model used. The model allows strictly controlled crossover studies on the effects of drugs on signs and symptoms associated with a soft tissue and bone injury.²⁻⁹

We studied whether homoeopathy would significantly affect pain and other events after surgical intervention.

Subjects and methods

The experimental design was on a randomised double blind, crossover basis using patients with bilaterally impacted lower wisdom teeth. This allowed two separate and "identical" operations in each patient. Assessments were made for a paired comparison of pain and other events during the two

postoperative courses: treatment with homoeopathy or placebo.

PATIENTS

With approval from the regional Committee on Medical Research Ethics, 24 healthy outpatients (20 women and four men; mean (range) age 24 (19 to 28) years volunteered after they had received oral and written explanation of the events and implications of the trial. They all needed prophylactic surgical removal of identical bilaterally impacted mandibular third molars, as evaluated clinically and by means of orthopantomograms. The patients were highly motivated for the trial, 14 being students in the Norwegian Academy of Natural Medicine. There was no drop out.

SURGERY

The two operations were performed by the same surgeon (PS) at the same time of the day, and, with two exceptions, on the same day of the week. The mean (range) interval was 27 (14 to 51) days. Surgery was performed by a standardised technique.⁴ Before each operation 5.4 ml local anaesthetic (20 mg lignocaine plus 12.5 µg adrenaline/ml: Astra, Sweden) was injected. The time from injection to last suture averaged 10.3 minutes (range 8 to 13) for the operation followed by placebo treatment and 10.2 minutes (range 8 to 14) when followed by homoeopathy.

HOMOEOPATHIC TREATMENT

Classic homoeopathy is based on individualised treatment with a single drug selected according to the signs and symptoms of the patient. Six homoeopathic drugs were chosen as the most likely alternatives: *arnica*, *hypericum*, *staphisagria*, *ledum*, *phosphorus*, and *plantago*. They were prepared at the D30 potency according to accepted requirements for homoeopathic remedies and used for medication of sucrose tablets.¹⁰ Identical sucrose tablets served as placebo. The drugs were supplied in vials of 100 tablets (Vala Pharma Laboratorium AB, Gothenburg, Sweden). For each patient one set with six vials containing homoeopathic tablets (*arnica*, *hypericum*, etc) and one with six vials containing placebo tablets (also labelled *arnica*, *hypericum*, etc) were coded. Treatments were allocated according to a block randomisation system (four patients in each block), which ensured that half of the patients received placebo after the first operation. The study was double blind as neither the clinical investigators nor the patients had any access to the randomisation list.

Treatment started three hours after completion of surgery with the remedy selected by the homoeopaths. Each dose consisted of three tablets. One dose was administered quarterly for the first three hours, thereafter one dose per hour until bedtime, and two doses the following morning at an interval of three hours. Twenty four hours after treatment was initiated, the signs and symptoms of the patient were re-evaluated by the homoeopaths. Thereafter treatment continued with four doses before bedtime, either with the first choice or an alternative from the same set of vials.

Section of Dental Pharmacology and Pharmacotherapeutics, University of Oslo, 0316 Oslo, Norway
Per Lökken, professor

Saint Hanshaugen Medical Centre, 0168 Oslo, Norway
Per Atle Straumsheim, homoeopath

Norwegian Institute for Natural Medicine, 1340 Bekkestua, Norway
Dag Tveiten, homoeopath

Section of Maxillofacial Surgery, Oslo City Hospital, 0407 Oslo, Norway
Per Skjelbred, chief surgeon

Department of General Practice, University of Oslo, 0264 Oslo, Norway
Christian Fredrik Borchgrevink, professor

Correspondence to: Professor Borchgrevink, Fr. Stangs gt 11/13, 0264 Oslo, Norway.

BMJ 1995;310:1439-42

FIG 1—Device for measurement of swelling in jaw region

Three doses were then given daily for the next five days.

OTHER DRUGS

If an analgesic was greatly needed, the patients were allowed to take codeine tablets (codeine phosphate 25 mg) and the intake was recorded. No other drug was permitted in the period of observation.

ASSESSMENTS

Pain was rated on a visual analogue scale with lines from "no pain" (0 mm) to "pain cannot be worse" (100 mm), with 28 assessments after each operation, five of which were made before start of treatment (see fig 2). Facial swelling at the site of surgery was measured with a mechanical device (fig 1) which gives a measurement of the postoperative swelling by subtraction of recordings before operation from those afterwards.² The maximum ability to open the mouth (distance between the edges of upper and lower incisors) was measured with a vernier gauge.² On days 3 and 7 after surgery the patients were also examined for complications in wound healing and discolouration indicative of haematoma or ecchymoses.⁴ Postoperative bleeding was assessed according to the criteria indicated in table III. On each evening after the operation the patients recorded any special discomfort.

After the second operation, the patients gave an overall assessment of preference for postoperative course on a visual analogue scale with a line from "maximum preference for the first course" (0 mm) to "maximum preference for the second course" (100 mm). They were invited to state or guess after which operation they had received homoeopathic treatment. The patients indicated their attitude to and trust in homoeopathy on a visual analogue scale from "no confidence in homoeopathy" (0 mm) to "maximum confidence in homoeopathy" (100 mm), both before and at the end of the trial.

STATISTICAL METHODS

For pain, trismus, swelling, and bleeding the difference between the values after treatment for homoeopathy and placebo was analysed by using analysis of covariance (ANACOVA) with adjustment for period effects and for correlation with pretreatment values.¹¹ When several measurements were made before and after treatment their mean was used.¹² Due to skewness, the visual analogue score for pain was logarithmically transformed before analysis. For pain, the pretreatment mean was analysed (ANACOVA) to test for carry over effects given period effects. ANOVA was used to test the preference of patients for each treatment and period effect. Binominal tests were used to check for shifts in dichotomous variables away from the 50-50 distribution. All tests were two sided, and P

values below the 5% level were regarded as significant. Treatment effects were estimated and other effects were estimated when significant. Estimates are given with 95% confidence intervals.

Results

The first choice of homoeopathic treatment in the 24 patients was arnica for nine, phosphorus for seven, hypericum for five, ledum for one, staphisagria for one, and plantago for one. When re-evaluated on day 1 after surgery the choice was arnica for 21, phosphorus for two, and ledum for one. The first choice when placebo was actually given was arnica for 12, phosphorus for six, hypericum for four, and staphisagria for two, and when re-evaluated it was arnica for 20 and phosphorus for four.

Pain—Postoperative pain was essentially the same whether the patients were treated with homoeopathy or placebo (fig 2). The mean estimated pain for the

FIG 2—Mean pain assessments by visual analogue scales (VAS) after two separate "identical" oral surgical interventions in a crossover trial in 24 patients in whom placebo or homoeopathic treatment started 3 hours after surgery (no pain=0 mm; pain cannot be worse=100 mm). A: assessments on day of surgery; B: assessments on day 1-7 after surgery (m=morning, e=evening)

entire treatment period was 2% greater with homoeopathy as compared with placebo (95% confidence interval -27% to 42%; $P=0.90$). Codeine tablets were taken by seven patients. A total of 23 tablets were taken when patients were treated with homoeopathy and 16 tablets were taken during placebo treatment. One patient accounted for 18 tablets, of which 14 were taken during homoeopathic treatment.

Swelling and trismus—Twelve patients had greater swelling with homoeopathy and 12 with placebo (table I). Compared with placebo there was 33% less reduction in ability to open the mouth on day 3 with homoeopathy (table II), a difference of borderline significance ($P=0.05$).

Bleeding—Essentially there was no difference in bleeding after the two operations (table III). Eight patients exhibited haematoma or ecchymoses at the site of surgery; five after both operations, two only when treated with homoeopathy, and one only when treated with placebo.

Side effects and complaints—Wound healing was uneventful in all patients after both operations. Non-specific complaints (for example, headache, dizziness) were recorded by five patients after each operation, mostly on the evening after surgery and by the same patients after both operations.

Preference for and confidence in homoeopathy—Homoeopathy was favoured by 11 and placebo by 13

TABLE I—Swelling after two "identical" oral surgical interventions in a crossover trial in 24 patients treated with placebo and homoeopathy

Day after surgery	No of patients with swelling			Mean amount of swelling (mm)		
	Less after homoeopathy	Same	Less after placebo	Homoeopathy	Placebo	Difference (95% confidence interval)
3rd	12	0	12	18.7	19.7	-1.0 (-7.5 to 5.5)
7th	13	1	11	6.7	4.9	1.8 (-0.7 to 4.3)

TABLE II—Reduction in ability to open mouth (trismus) after two "identical" oral surgical interventions in a crossover trial in 24 patients treated with placebo and homoeopathy

Day after surgery	No of patients with trismus			Mean trismus (mm)		
	Less after homoeopathy	Same	Less after placebo	Homoeopathy	Placebo	Difference (95% confidence interval)
3rd	12	4	8	6.7	10.1	-3.4 (-6.7 to 0.0)
7th	11	5	5	3.7	5.8	-2.1 (-4.6 to 0.4)

TABLE III—Bleeding after two “identical” oral surgical interventions in a crossover trial in 24 patients treated with placebo and homoeopathy

Time after surgery	No of patients reporting bleeding			Mean scores for bleeding*	
	Less after placebo	Same	Less after homoeopathy	Placebo	Homoeopathy†
4 hours	5	13	6	1.6	1.5
1st evening	7	11	6	1.1	1.7
2nd evening	5	13	6	1.0	0.8
3rd evening	4	14	6	0.4	0.3
4th evening	6	14	4	0.3	0.3
5th evening	2	21	1	0.1	0.1
6th evening	2	21	1	0.1	0.1

*Scores: 0 = none, 1 = taste of blood, 2 = some blood in mouth, 3 = much blood in mouth.

†Non-significant increase in bleeding with homoeopathy; estimated strength 0.02 on the ordinal scale from 0 to 3 (95% confidence interval -0.26 to 0.29; P=0.86).

patients (fig 3). There was a non-significant preference for placebo: 0.2 mm (95% confidence interval -15.6 mm to 16.0 mm; P=0.98). Eleven of the 24 patients correctly indicated or guessed after which operation they had received homoeopathic treatment. The high confidence of the patients in homoeopathy remained essentially unchanged: mean score 79 mm (range 50 to 100) before and 82 mm (range 37 to 100) after the trial.

FIG 3—Overall preference of patients for postoperative course assessed after second operation. Abscissa: assessment by 100 mm visual analogue scale. (Maximum preference for homoeopathy = -50 mm. No difference = 0 mm. Maximum preference for placebo = 50 mm). Ordinate: each patient ranked according to preference

Period and carry over effects—Statistical analyses revealed significant period effects in pain and trismus before treatment but no significant carry over effect. A period effect is a general change in response from the first to the second period, whereas a carry over effect means that the effect of a treatment in the first period lasts and changes the response in the second period. Pain before treatment after the second operation was 40% lower compared with the first operation (95% confidence interval 9% to 61%; P=0.02). During treatment, the assessment of pain showed a weaker period effect, which became insignificant when adjusted for values before treatment (P=0.32). The mean ability to open the mouth was virtually the same before the two operations (48.4 mm v 48.6 mm). After the operations, however, there was a significant period effect, with less trismus after the second operation. Difference on day 3 was 5.9 mm (2.5 mm to 9.2 mm; P=0.001) and on day 7 was 3.3 mm (0.8 mm to 5.9 mm; P=0.01).

Discussion

The review of clinical trials in homoeopathy by Kleijnen *et al* refers to 20 studies on trauma and pain.¹ In 18 of these, the outcome was interpreted as positive by the authors. Our results, however, indicated no significant effect of homoeopathy on pain and other events after an acute soft tissue and bone injury. In fact, the postoperative course with placebo was remarkably similar to that with homoeopathy (figs 2 and 3). This is in contrast with previous placebo controlled trials on analgesic and anti-inflammatory

drugs in this clinical model, which have all shown significant differences.^{2,3,5-9} The power of the present trial was, however, reduced by the lower pain scores of these patients. As seen from the confidence intervals, a relative difference of about 30% to 40% would have been needed for an effect to become significant.

Generally, small sample sizes will affect power—that is, the probability of detecting small effects—and is a particular problem with negative findings. Power calculations indicate that detection of a 5% relative difference would have required a crossover study in about 1000 patients (that is, 11 000 visits by the patients to the surgeon and the homoeopaths). The lack of any trend in figures 2 and 3 indicating a possible effect of homoeopathy suggests that even a large scale trial with many patients and accordingly greater power would probably not change the validity of our negative findings. Practically, attainment of clinical proof for the non-existence of a homoeopathic effect is impossible.

As the effects of treatment are claimed to last for long periods, crossover studies on homoeopathy should be examined for carry over effects.^{1,13} Our analyses found no significant carry over effect, but the estimate is rather insensitive, being based on comparison between patients.

Homoeopathic treatment is selected on an individual basis. The few individualising symptoms in the patients (for example, low pain) made it difficult to choose the most appropriate homoeopathic medicine. Not surprisingly, 21 of the 24 patients ended up with arnica. Arnica is recognised by homoeopaths as the remedy par excellence for wounds and injuries,¹⁴ not least to reduce the effects of dental surgery.¹³⁻²² The present potency (D30) represents a medium potency (dilution 1: 10³⁰) often used in homoeopathy. Perhaps a higher potency could have been more appropriate as several authors have recommended higher potencies of arnica for treating trauma and pain.^{16-18,20-22} In two pilot trials on arnica as a remedy for injuries, Campbell found arnica ineffective in a dilution of C30 (1:10⁶⁰) but apparently effective in a dilution of 10 M (1:10^{20 000}).¹⁶ This would agree with homoeopathic theory, according to which a higher potency is expected to be more effective than a lower one.

Buckman, in a recent discussion in the *BMJ* on “What does homoeopathy do—and how?” pointed out that, besides evidence and mechanism, the important issue is whether patients feel better when they take homoeopathic remedies.²³ The pain scores of our patients were remarkably low after both operations. Despite inability to identify correctly the postoperative course with homoeopathic treatment, their strong confidence in homoeopathy remained unchallenged. Conventional physicians and devoted homoeopaths cooperated without problems in this study. The physicians believe that the low pain scores and satisfaction of the patients may at least partly reflect the clinical skill of the two homoeopaths.

Key messages

- There is growing use of homoeopathy but equivocal evidence of efficacy
- This crossover trial studied the effects of homoeopathy on pain and other events of removal of impacted wisdom teeth
- Remarkably similar assessments of pain were observed with homoeopathy and placebo
- No positive evidence could be found for homoeopathic effects

We acknowledge the Norwegian Research Council for funding this work. Homeopathic drugs and corresponding placebo tablets were kindly supplied free of charge by Vala Pharma Laboratorium AB (Gothenburg, Sweden). E A Rödland (Medstat Research, Lilleström, Norway) performed the statistical analyses.

- 1 Kleijnen J, Knipschild P, Riet ter G. Clinical trials of homeopathy. *BMJ* 1991;302:316-23.
- 2 Lökken P, Olsen I, Bruaset I, Norman-Pedersen K. Bilateral surgical removal of impacted lower third molar teeth as a model for drug evaluation: a test with ibuprofen. *Eur J Clin Pharmacol* 1975;8:209-16.
- 3 Album B, Olsen I, Lökken P. Bilateral surgical removal of impacted lower third molar teeth as a model for drug evaluation: a test with oxphenbutazone (Tanderil). *Int J Oral Surg* 1977;6:177-89.
- 4 Skjelbred P, Album B, Lökken P. Acetylsalicylic acid vs paracetamol: effects on postoperative course. *Eur J Clin Pharmacol* 1977;12:257-64.
- 5 Lökken P, Skjelbred P. Analgesic and anti-inflammatory effects of paracetamol evaluated by bilateral oral surgery. *Br J Clin Pharmacol* 1980;10:27-33.
- 6 Skjelbred P, Lökken P. Phenazone versus placebo: effects on post-operative course. *Eur J Clin Pharmacol* 1980;18:327-31.
- 7 Skjelbred P, Lökken P. Post-operative pain and inflammatory reaction reduced by injection of a corticosteroid: a controlled trial with bilateral oral surgery. *Eur J Clin Pharmacol* 1982;21:391-6.
- 8 Skjelbred P, Lökken P. Effects of naloxone on post-operative pain and steroid-induced analgesia. *Br J Clin Pharmacol* 1983;15:221-6.
- 9 Skjelbred P. The effects of acetylsalicylic acid on swelling, pain and other inflammatory events after surgery. *Br J Clin Pharmacol* 1984;17:379-84.
- 10 *Homöopathisches Arzneibuch*. 1st ed (Amdtliche Ausgabe). Stuttgart: Deutscher Apotheker Verlag, 1978 (with five revisions up to 1991).

- 11 Jones B, Kenward MG. *Design and analysis of cross-over trials*. London: Chapman and Hall, 1989.
- 12 Frison L, Pocock SJ. Repeated measures in clinical trials: analysis using mean summary statistics and its implications for design. *Stat Med* 1992;11:1685-1704.
- 13 Righetti M. *Forschung in der Homöopathie. Wissenschaftliche Grundlagen, Problematik und Ergebnisse*. Göttingen, Germany: Ulric Burgdorf-Verlag für homöopathische Literatur, 1988.
- 14 Gibson DM. Arnica, a study. *British Homeopathy Journal* 1972;61:167-70.
- 15 McIvor EG. A clinical trial following surgery and trauma. *Journal of American Institute for Homeopathy* 1973;66:81-4.
- 16 Campbell A. Two pilot controlled trials of arnica montana. *British Homeopathy Journal* 1976;65:154-8.
- 17 Ives G. A double blind pilot study of Arnica in dental extraction. *Communications of the Midlands Homeopathy Research Group* 1984;11:71-4.
- 18 Albertini H, Goldberg W, Sanguy BB, Toulza C. Homeopathic treatment of dental neuralgia using arnica and hypericum: a summary of 60 observations. *Journal of American Institute for Homeopathy* 1985;78:126-8.
- 19 Kaziro GSN. Metronidazole (Flagyl) and arnica montana in the prevention of post-surgical complications, a comparative placebo controlled clinical trial. *Br J Oral Maxillofac Surg* 1984;22:42-9.
- 20 Pinsent RJFH, Baker GPI, Ives G, Davey RW, Jonas S. Does arnica reduce pain and bleeding after dental extraction? A placebo controlled pilot study conducted by the Midland Homeopathy Research Group (MHRG) in 1980/81. *Communications of the British Homeopathic Research Group* 1986;15:3-11.
- 21 Meuris J. *Homéopathie en odonto-stomatologie*. 3rd ed. Bordeaux: 1981.
- 22 Lessell CB. *The dental prescriber*. London: The British Homeopathic Association, 1983.
- 23 Buckman R, Lewith G. What does homeopathy do—and how? *BMJ* 1994;309:103-6.

(Accepted 11 April 1995)

Patients with major trauma who do not use emergency ambulances

B P McNicholl, J Lee

Accident and Emergency Department, Royal Victoria Hospital, Belfast BT12 6BA
B P McNicholl, research fellow
J Lee, senior house officer

Correspondence to:
Dr McNicholl.

BMJ 1995;310:1442

When planning a trauma service it is important to estimate the number of injured patients who will attend a hospital other than the designated trauma centre. Up to a third of patients in one study went to the wrong hospital.¹ This happens because paramedics make triage errors and take patients to the wrong hospital² and (we hypothesise) because some patients make their own way to hospital. Because a trauma service may be established in Northern Ireland we tried to estimate the numbers of injured patients likely to take themselves to the wrong hospital.

Methods and results

For one year a surveillance system monitored 12 randomly chosen hospitals out of the 19 in Northern Ireland that receive cases of major trauma. Patients were detected by monitoring all the accident and emergency and intensive care units, tertiary referral centres, and necropsies. Patients with an injury severity score of >15 who reached hospital alive were included. Data were collected by twice weekly monitoring of each hospital and the ambulance service (where all emergency calls are tape recorded). We collected data on how each patient had arrived at hospital.

Of 239 patients in the study 39 (34 men, 5 women) did not arrive at hospital by ambulance (see table). Thirty one patients went to their nearest hospital. Their median injury severity score was 24, and five died. Seven injuries were penetrating. Half of the patients (20) required immediate surgery (defined as surgery for life threatening injury to vessels or organs scoring abbreviated injury score of 3 or more), nine neurosurgical procedures, and eight laparotomies. Among the 200 patients who did use emergency ambulances 44 (22%) required immediate surgery ($\chi^2=00.00$; $P<0.001$).

Seventeen patients had a delay between injury and transport to hospital. This was due to delays in the appearance of physical signs and delays in acting on them by relatives or general practitioners. Ten of these patients were injured in falls at ground level and were not found for some time or treated as drunk.

Comment

Studies from the United States have shown that between 7% and 21% of all trauma victims may be taken to the wrong hospital by the paramedics staffing emergency ambulances.^{2,3} If even trained paramedics make wrong decisions then patients themselves might be likely to. Moreover, patients cannot be expected to know which hospitals are trauma centres and which are not. Our study showed that even in a place with a free emergency ambulance service, 16% of badly injured patients make their own way to hospital.

These findings suggest that within a planned trauma service, with designated trauma centres, any hospital with an accident and emergency department, whether a trauma unit or not, should be prepared to receive critically injured patients unexpectedly. Based on our data and those from the United States the proportion may be anywhere between 7% and 37% (though not all the patients who make their own way to hospital will go to the wrong one). The likely size of this group, the relative fate of these "outcasts," and whether a higher morbidity among this group offsets the benefits of trauma centres need to be prospectively researched. In both predicting and evaluating the effectiveness of a trauma service these patients need to be included in the calculations.

We thank the Department of Health for funding and Mr W H Rutherford and Mr B Fisher for their advice. We are grateful to the Northern Ireland ambulance service and the participating hospitals for their cooperation.

- 1 Mackenzie EJ, Steinwachs DM, Ramzy AI. Evaluating performance of statewide regionalized systems of trauma care. *J Trauma* 1990;30:681-8.
- 2 Knudson P, Frecceri CA, DeLateur SA. Improving the field triage of major trauma victims. *J Trauma* 1988;28:602-6.
- 3 West JG, Murdock MA, Baldwin LA, Whalen E. A method for evaluating field triage criteria. *J Trauma* 1986;26:655-9.

(Accepted 11 April 1995)

Mode of transport to hospital by those patients who did not arrive in an emergency ambulance

	No
Unknown*	14
Car	14
Other ambulance†	6
Carried	2
Police	2
Bus‡	1
Total	39

*These patients did not have mode of transport recorded in their hospital records, but we know they did not use emergency ambulances.
†Two of these were requested by family doctors.
‡An injured bus driver.