Double-blind, placebo-controlled, randomized clinical trial of homoeopathic arnica C30 for pain and infection after total abdominal hysterectomy

Oliver Hart[1] Mark A Mullee MSc CStat[2] George Lewith DM MRCP[3] John Miller DM FRCOG

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SUMMARY

Homoeopathic potencies of arnica have been used for many years to aid postoperative recovery. The effects of arnica C30 on pain and postoperative recovery after total abdominal hysterectomy were evaluated in a double-blind, randomized, controlled study.

Of 93 women entered into the study, 20 did not complete protocol treatment: nine were excluded because they failed to comply with the protocol, nine had their operations cancelled or changed within 24 h and two had to be withdrawn because of the recurrence of previously chronic painful conditions. Those who did not complete protocol treatment were equally divided between the arnica (nine patients) and placebo groups (11 patients). 73 patients completed the study, of whom 35 received placebo and 38 received arnica C30. The placebo group had a greater median age and the arnica group had slightly longer operations; nevertheless, no significant difference between the two groups could be demonstrated.

We conclude that arnica in homoeopathic potency had no effect on postoperative recovery in the context of our study.

INTRODUCTION

Although there are many documented cases of individual homoeopathic success, there have been few high quality clinical trials of homoeopathy. Kleijnen *et al.*[1] reviewed 107 trials dating back to 1943. 81 of these studies reported results that favoured homoeopathy and 24 trials found homoeopathy to be ineffective. Considering the low quality of most of these studies, particularly the randomization, Kleijnen *et al.* concluded that 'the evidence of clinical trials is positive but not sufficient to draw a definitive conclusion'. It is of note that 15 of 22 of the best designed studies suggested that homoeopathy did have a positive effect.

A review of the published work on arnica reveals that there are nine clinical trials looking at the effects of arnica in trauma; four of these were inconclusive[2–5]. Arnica in homoeopathic potency has traditionally been utilized by homoeopaths to treat bruising. Campbell[6] showed that arnica 10 M was effective in reducing bruising in an experimental pilot study. Arnica C30 appeared ineffective when compared to placebo. Campbell's trial was not randomized, although a crossover design was employed. All patients received placebo first and arnica second; it may be that the second bruise was not as severe as the first, or perhaps there was some form of accommodation. Furthermore, Campbell's trial size was very small, 13 individuals in the 10 M study and 10 in the 30C study[6]. In a randomized, double-blind, placebo-controlled crossover study of homoeopathic drugs each prescribed on an individual basis (arnica, hypericum, staphisagria, ledum, phosphorus and plantago at D30 potency) to patients undergoing oral surgery, Lökken *et al.*[7] demonstrated a significant effect from individualized homoeopathy on trismus alone. Trismus was one of only four outcome variables, the others being wound healing, pain and postoperative bleeding. None of the other variables showed a significant change in response to homoeopathy. However, Lökken's study does suggest that appropriately prescribed homoeopathy may have an effect on tissue trauma. Kaziro compared arnica to metronidazole and placebo in reducing post-surgical pain, oedema and wound healing following dental surgery[8]. Arnica proved significantly less effective than metronidazole. In a similar study Pinsent *et al.*[9] found that arnica C30 could reduce both pain and bleeding in a statistically significant manner after dental extraction, although their statistical analysis is questionable. The study

[1]Medical Student, [2]Medical Statistics and Computing, and [3]Department of Medicine, University of Southampton; [4]Department of Obstetrics and Gynaecology, Princess Anne Hospital, Southampton, England

Correspondence to: Dr George Lewith, University Medicine, Level D (810), Centre Block, Southampton General Hospital, Tremona Road, Southampton SO16 6YD, England

was considered a pilot despite entering 100 patients, 72 of whom completed the trial. The authors themselves felt that there were problems in relation to pain recording, dental anaesthesia, and matching the patients for age and sex. Gibson *et al.*[10] conducted a small double-blind placebo-controlled trial of arnica in acute trauma patients who were slow to make progress. They reported that those patients receiving arnica C30 showed a significant advantage in both objective and subjective parameters. Differences between the two groups were dramatic, but only 20 patients were entered. Gibson *et al.* obtained significance by counting the number of outcome measures in which arnica was superior to placebo and then applying a binomial test. This test assumes that observations are independent, an assumption clearly incorrect in this case. Therefore, although Gibson's study does suggest that arnica may be of value, the conclusions are based on questionable statistical analysis. Tetau[11] reported a double-blind study of the haemostatic properties of arnica in 5C potency. He suggested that those receiving arnica experienced changes in their haemostatic indices, including platelet aggregation and blood clotting. 39 patients were involved; the result was statistically significant and implies a mechanism through which arnica may have an effect. A larger study by Baillargeon *et al.*[12] did not replicate Tetau's observations.

Arnica has been consistently recommended by homoeopathic practitioners as a treatment for bruising and trauma. It is also used widely in clinical practice just before and immediately after major operative interventions, with the aim of aiding recovery and reducing pain and bruising. We therefore chose to evaluate this empirical use of arnica in the model of postoperative recovery after elective total abdominal hysterectomy.

METHOD

All patients booked for total abdominal hysterectomies at the Princess Anne Hospital, Southampton, between January and March 1995 were approached by post with details of the trial and some background information about homoeopathy. Patients entered the hospital 24 h preoperatively and during this time they were recruited and randomized. Two doses of arnica C30 or placebo were taken in the 24 h preoperatively and then three doses each day for 5 days postoperatively starting on the morning after the operation.

The arnica C30 and placebo were prepared by Ainsworth Pharmaceuticals, a registered UK homoeopathic manufacturer. The placebo comprised unmedicated plain white tablets. The tablets containing the active homoeopathic preparation looked exactly the same and were prepared in accordance with the rigorous guidelines laid down by the Blackie Foundation. Tablets were delivered in bulk to the Centre for the Study of Complementary Medicine in Southampton, and then dispensed into individual numbered bottles according to the prearranged randomization code. It was impossible for the investigator or the trial participants to identify whether the tablets were placebo or real treatment. Randomization codes were generated by computer program. Patients were then provided with the next numbered medication bottle from a coded pack on entry into the study.

The choice of homoeopathic potency was a complex one. Pinsent *et al.*, in the largest positive trial involving arnica, used a C30 potency[9]. Hofmeyr[5] used a D6 potency, but that study had fewer patients and the result was not statistically significant. A consensus view was therefore taken among homoeopaths that, along with the clinical trial evidence, led us to choose a 30C potency in this experiment. To measure the efficacy of arnica versus placebo, several outcome measures were employed. *Pain and discomfort* were measured by standard 10 cm visual analogue scales completed every 12 h, beginning 12 h after the operation. A maximum of 10 assessments per patient were completed. The *length of operation*, *estimated blood loss* and *difficulty of operation* were recorded. The surgeon was asked to estimate whether the procedure was easy, difficult or very difficult (1, 2 or 3, respectively). *The presence of infection* was defined as the clinical need to prescribe antibiotics (over and above prophylaxis). A careful record was kept of the simple *analgesics*, non-steroidal anti-inflammatories and opioids used in each individual patient. The opioids were provided by patient controlled intravenous infusion (PCA). The primary investigator (OH) assessed the patients' *anxiety* about their forthcoming procedure at entry into the study. This was a simple clinical observation; patients rated one star were very anxious and those rated three appeared very relaxed about the procedure. After hospital discharge, each patient was followed up by telephone 2 weeks after the procedure and asked if she had any *residual pain*, difficulty or complication as a result of the hysterectomy.

Statistical comparisons between the groups were performed by Mann–Whitney U tests, chi-square tests and ANCOVA (analysis of covariance). Adjusted means were computed by general factorial analysis of variance. Comparisons between the two groups of pain scores over time were made by computing summary measures, such as rate and the area under the curve, as described by Matthews *et al.*[13] The data were analysed by use of SPSS for Windows (version 6.1)[14]. Data were analysed blindly with respect to treatment allocation.

RESULTS

Of the 93 women recruited into the study, 20 did not complete protocol treatment. Of these, nine were excluded because they failed to comply (i.e. did not take their medication as directed), nine had their operations cancelled

Table 1 **Comparison of baseline characteristics**

Variable	*Treatment*	n	*Median*	*Range*	*95% CI for the difference (arnica–placebo)*	z	P
Age (year)	Arnica	38	40	25–53			
	Placebo	35	43	32–76	−7–1	1.5	0.14
Estimated blood loss (mL)	Arnica	38	300	50–1500			
	Placebo	33	300	50–850	0–150	1.16	0.25
Length of operation (min)	Arnica	38	80	40–200			
	Placebo	35	75	40–120	−5–20	1.33	0.19
Days in hospital	Arnica	38	6	5–11			
	Placebo	35	6	5–11	−1–0	0.94	0.35
Surgeon's severity score	Arnica	38	1	1–3			
	Placebo	34	1	1–3	0–0	1.18	0.24
Score for positivity	Arnica	38	2	1–3			
	Placebo	35	2	1–3	0–0	0.48	0.64
Visual analogue score	Arnica	38	59	0–94			
(morning after operation)	Placebo	35	41	3–99	0––21	1.9	0.06
Anaesthetic type	Arnica	Placebo				χ^2	
Fentanyl/propofol	40%	57%					
Thiopentone/propofol	42%	37%					
Other	18%	6%				3.69	0.16
Diagnosis							
Dysmenorrhoea	18%	9%					
Menorrhagia	32%	37%					
Both	18%	20%					
Abnormal smear	10%	9%					
Fibroids	18%	9%					
Other	13%	17%				1.75	0.88

or changed within 24 h and two had to be withdrawn because of the recurrence of previous chronically painful conditions (back pain). Those who did not complete protocol treatment were divided equally between arnica (nine patients) and placebo (11 patients).

Baseline characteristics

Of the 73 patients completing protocol treatment, 35 received placebo and 38 received arnica C30. Table 1 shows baseline characteristics. The placebo patients had a higher median age whereas the median length of operation was longer in those patients receiving arnica. There is a suggestion that anaesthetic type varied between the two groups ($\chi^2 = 3.69$, df = 2, $P = 0.16$), but diagnosis was quite comparable ($\chi^2 = 1.75$, df = 5, $P = 0.88$). The groups also had comparable surgeon's severity score and scores for positivity (estimation of preoperative anxiety).

A consistent element of homoeopathic tradition is that appropriately prescribed remedies may aggravate a condition before clinical improvement. Whilst not a baseline characteristic, the visual analogue score taken on the morning after the operation is of interest since there is a suggestion of homoeopathic aggravation before a subsequent improvement. The median pain score was certainly higher for the arnica group than for the placebo group, although this did not reach statistical significance.

Outcome measures

The infection rate, as defined by the need for the prescription of systemic antibiotics, was 76% (29) for the arnica group and 71% (25) for the placebo group. This small difference was not significant [$\chi^2 = 0.22$, df (degrees of freedom) = 1, $P = 0.63$, 95% CI (confidence interval) for difference in proportions −15% to 25%]. The median time spent in hospital was 6 days for both groups. 62% (23)

Table 2 **Comparison of total analgesic use**

Drug intake (totals)	*Treatment*	n	*Median*	*Range*	*95% CI for the difference (arnica–placebo)*	z	P
Opioids (mg)	Arnica	38	70	11–130			
	Placebo	35	68	20–229	−14 to14	0.12	0.90
Co-proxamol (doses)	Arnica	38	10	0–17			
	Placebo	35	8	0–13	−1 to 4	1.03	0.30
Temazepam (mg)	Arnica	38	30	0–100			
	Placebo	35	20	0–80	−20 to 10	0.17	0.87
Antiemetics (dose)	Arnica	38	1	0–5			
	Placebo	35	2	0–6	−1 to 10	1.04	0.30
Diclofenac (doses)	Arnica	38	2	0–12			
	Placebo	35	2	0–9	−1 to 1	0.48	0.63
Non-steroidal anti-inflammatory	Arnica	38	0	0–11			
(doses—excluding diclofenac)	Placebo	35	0	0–13	0 to 0	0.54	0.59

arnica patients and 66% (23) placebo patients were still experiencing pain at 2-week follow-up. This slight difference of 4% in favour of the arnica group was not significant ($\chi^2 = 0.1$, df = 1, $P = 0.75$, 95% CI = −26% to 19%).

Analgesics

The arnica patients had higher total opioid and temazepam intake but lower antiemetic doses; none of these differences was statistically significant (Table 2). Analysis of covariance, adjusting for age, estimated blood loss and length of operation also revealed no statistically significant differences in analgesic intake between the groups.

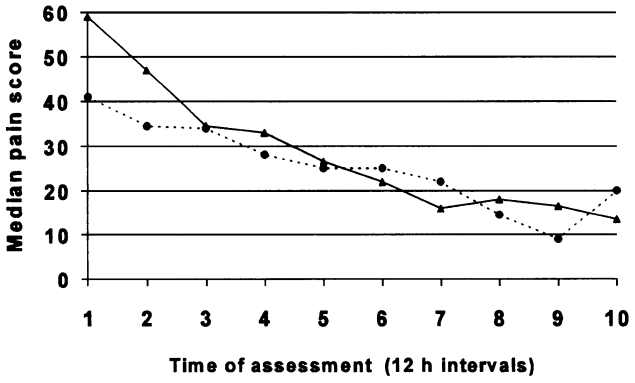

Figure 1 **Comparison of median pain score during the study**

Pain scores

Figure 1 indicates the trend in pain scores during the period of the study. It should be noted that only 12 arnica and 10 placebo patients recorded pain scores at the tenth assessment after the operation. In accordance with the recommendation of Matthews *et al.*[13], separate graphs of pain scores against time were plotted for each patient. To demonstrate the variety of plots obtained, 10 of these graphs (five from each group) were randomly selected, and are displayed for illustrative purposes in Figure 2. Two of the authors (MM and GL) examined all the individual charts independently (blind to treatment allocation), and tried to classify them into patients who showed an improvement or a deterioration in pain score over time. Several of the charts displayed irregular patterns of peaks and troughs in their pain scores, and it was sometimes difficult to discern a trend. 61% (23) of arnica patients and 66% (23) of placebo patients showed improvement; 8% (3) of arnica patients and 6% (2) of placebo patients showed a deterioration. The remaining charts indicated little change or were difficult to classify.

Summary measures to compare group pain scores over time are detailed in Table 3. The mean pain score and area under the curve suggest that the arnica patients had more pain than the placebo group during the period of the study. The rate of change and time to minimum score favoured the arnica patients, but none of these differences was statistically significant. Analysis of covariance was used to compare the summary measures between the groups after adjustment for age, surgeon's estimate of blood loss (minor, moderate or major) and length of operation (Table 4). There is some evidence that, after adjustment for all other variables in the model, the rate of change is greater in the arnica C30 group than in the placebo group. However, the adjusted means and 95% CI indicate that the other summary measures of mean pain score, area under the curve and time to minimum pain score are comparable between the groups.

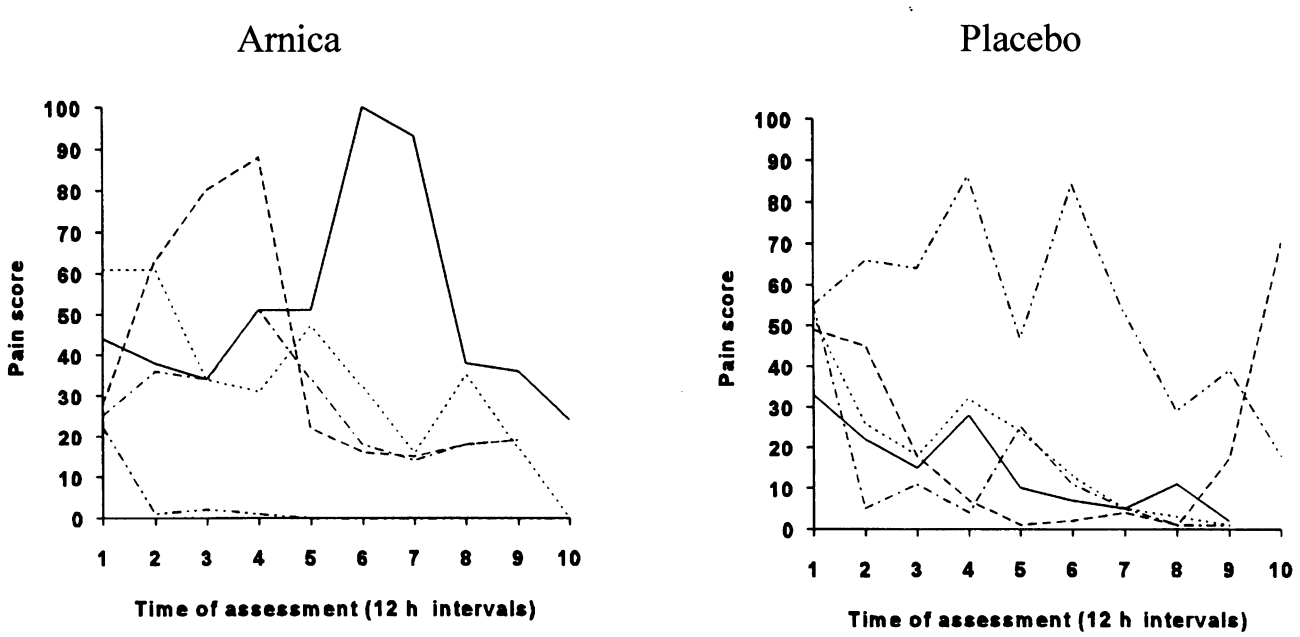

Figure 2 **Ten individual plots (five from each group) picked at random to demonstrate the variety of pain score against time after operation, observed for the 73 patients in the study.**

Table 3 **Summary measures used to compare group pain score over time. The rate of change was computed by fitting a linear regression to pain score versus time and using the slope as a summary measure. The area under the curve was calculated according to the trapezium rule[12]**

Variable	*Treatment*	n	*Median*	*Range*	*95% CI for the difference (arnica–placebo)*	z	P
Mean pain score	Arnica	38	38.1	2.6 to 63	−2.6 to 12.0	1.29	0.20
	Placebo	35	27.7	6.6 to 56.8			
Rate of change	Arnica	38	−0.36	−0.95 to 0.09	−0.19 to 0.04	1.28	0.20
	Placebo	35	−0.25	−0.64 to 0.71			
Time to minimum score (h)	Arnica	38	72	0 to 108	−12 to 12	0.39	0.70
	Placebo	35	84	0 to 108			
Area under the curve	Arnica	38	3096	180 to 5700	−432 to1104	0.85	0.40
	Placebo	35	2520	708 to 6216			

Table 4 **Analysis of covariance adjusted means for the treatment variable (placebo = 0 and arnica C30 = 1), adjusting for age, estimated blood loss and length of operation**

Summary measure	n	*Adjusted mean*		*ANCOVA adjusted mean difference (SE)*	*95% CI adjusted mean difference*	t	P-value
		Arnica	Placebo				
Mean pain score	71	32.6	31.0	1.61 (3.48)	−5.3 to 8.6	0.46	0.64
Rate of change	71	−0.32	−0.22	−0.12 (0.06)	−0.247 to 0.002	1.96	0.05
Time to minimum pain score (h)	71	72	70	2.18 (7.51)	−13 to 17	0.29	0.77
Area under the curve	71	3049	3084	−35.44 (373.24)	−781 to 710	0.10	0.92

DISCUSSION

In terms of pain, analgesia, infection and operative severity, this study revealed no significant differences between the arnica and placebo groups. The arnica group were slightly younger and had longer operations than the placebo group. These differences, coupled with the higher initial pain scores in the arnica patients, might have contributed to the marginally faster rate of recovery in the arnica group. Post-hoc analysis of covariance, excluding the initial pain scores from the calculation of the regression slopes, was performed to explore the influence of the initial pain scores on the rate of improvement in pain. Exclusion of just the first pain score had little effect on the adjusted mean, but exclusion of the first and second scores reduced the adjusted mean difference to -0.08 (95% CI $= -0.23$ to 0.07, $P = 0.30$). Whilst the unadjusted analysis favours the placebo group for mean pain score and area under the curve, the analysis of covariance indicates that the two groups are comparable.

Pinsent *et al.*[9], who reported the only positive study, freely admit that their methodology and statistics were flawed, and that their pain recording and follow-up were inadequate. Our study entered a relatively large number of patients, all of whom were followed up scrupulously. The groups are well balanced for most entry criteria other than age. Only the placebo group has patients over 55 years of age and these patients tended to have lower initial visual analogue scores. Those below 55 years had a greater spread (both high and low) of their initial visual analogue score. In future studies involving postoperative pain we recommend stratification by age to ensure that the groups are evenly balanced. One possibility, though less likely, is that the higher initial pain scores represent homoeopathic aggravation. When an individual displays such aggravations homoeopaths consider this represents a healing crisis which ultimately results in dramatic improvement. However, since we were unable to measure pain before the operation, we can do no more than hypothesize about the possibility of an aggravation. Since the two groups showed similar trends during their stay at hospital and at two weeks' follow-up, the concept of healing crisis would appear to have little substance in relation to overall outcome.

The study by Lökken *et al.*[7] is particularly fascinating. The summary of the paper indicates that homoeopathy had no benefit in dental pain, but closer analysis reveals less trismus in the homoeopathically treated group than in the placebo group. Wound healing and pain did not differ. It does seem that, in this study, arnica may have had an effect on tissue trauma as reflected in trismus. This notion is in accord with the homoeopathic indications for arnica as well as Campbell's work on bruising[6]; so future studies should focus more on tissue trauma and bruising than on pain and wound healing. Furthermore, routine analgesia may have masked any effect provided by arnica. If this is the case then the overall effects of arnica in the context of operative intervention are probably very small and certainly do not justify the introduction of arnica as a routine preoperative preparation or postoperative treatment.

The arnica dosage regimen may have been less than ideal. We have already outlined our reasons for choosing 30C arnica, but fully accept that the choice of potency in this study is based on limited information. Pinsent *et al.* used arnica only after the operative intervention; their regimen provided arnica 30C every 15 min for the first 45 min postoperatively (three doses) and thereafter 2-hourly for the next six doses[9]. We were unable to effect this dosage regimen and indeed believe it would be impractical in most situations after major surgery.

Almost all patients undergoing hysterectomy complained of postoperative 'wind pain'. Arnica is intended to relieve the pain and bruising that results from trauma, and any beneficial effects on the wound itself might have been masked by the patient's generalized postoperative abdominal discomfort. However, we would again argue that if arnica was having an effect, in the context of this operative intervention, its effect is marginal.

REFERENCES

1 Kleijnen J, Knipschild P, ter Riet G. Clinical trials of homoeopathy. *BMJ* 1991;**302**:316–23

2 Gibson J. Arnica, a study. *Br Homoeopath J* 1972;**61**:167

3 Savage J, Roe B. A double blind trial to assess the benefits of *Arnica montana* in acute stroke illness. *Br Homoeopath J* 1977;**66**:207–20

4 Savage J, Roe B. A further double blind trial to assess the benefit of *Arnica montana* in acute stroke illness. *Br Homoeopath J* 1978;**67**:210–22

5 Hofmeyr GJ, Piccioni V, Blauhof P. Post partum homoeopathic *Arnica montana*, a potency finding pilot study. *Br J Clin Pract* 1990;**44**:619–21

6 Campbell D. Two pilot controlled trials of *Arnica montana*. *Br Homoeopath J* 1976;**65**:154–8

7 Lökken P, Straucmsheim PA, Tveiten D, Skelbred P, Borchgrevink CF. Effect of homoeopathy on pain and other events after acute trauma: placebo controlled trial with bilateral oral surgery. *BMJ* 1995;**310**:1439–42

8 Kaziro GSN. Metronidazole 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

9 Pinsent RJ, Baker GP, Ives G, Davey RW. Does arnica reduce pain and bleeding after dental extraction? *Commun Br Homoeopath Res Group* 1986;**15**:3–11

10 Gibson J, Haslam Y, Laurenson L, Newman P, Pitt R, Robins M. Double-blind trial of arnica in acute trauma patients. *Commun Br Homoeopath Res Group* 1991;**21**:34–41

11 Tetau. Arnica and injury, double blind clinical study. *Homeopath Heritage* 1993;**18**:625–7

12 Baillargeon L, Drovin J, Desjardins L, Leroux D, Audet D. The effects of *Arnica montana* on blood coagulation. *Can Fam Physn* 1993;**39**:2362–7

13 Matthews JNS, Altman DG, Campbell MJ, Royston P. Analysis of serial measurements in medical research. *BMJ* 1990;**300**:230–5

14 Norusis MJ. *The SPSS Guide to Data Analysis for Release 4*. Chicago: SPSS, 1990