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Article *in* Plastic and Reconstructive Surgery · July 2016

DOI: 10.1097/PRS.0000000000002249

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Arnica Ointment 10% Does Not Improve Upper Blepharoplasty Outcome: A Randomized, Placebo-Controlled Trial

Denise C. E. van Exsel, M.D.
Shariselle M. W. Pool, M.D., Ph.D.
Jeroen H. van Uchelen, M.D.
Mireille A. Edens, Ph.D.
Berend van der Lei, M.D., Ph.D.
Wynand B. W. H. Melenhorst, M.D., Ph.D.

Zwolle, Utrecht, and Groningen, The Netherlands

Background: It has been suggested that arnica can reduce postoperative edema and ecchymosis associated with cosmetic surgical procedures and improve outcome. Despite a high incidence of arnica use among upper blepharoplasty patients, evidence to support its treatment effect is lacking. The authors performed a randomized, double-blind, placebo-controlled trial to investigate the efficacy of arnica ointment after upper blepharoplasty.
Methods: One hundred thirty-six bilateral upper blepharoplasty patients were randomized between arnica ointment 10% and placebo ointment. In both study arms, one periorbital area was designated as the treatment side (either arnica or placebo ointment), and the contralateral side served as an untreated (no ointment) internal control. As the primary endpoint, the overall periorbital appearance as based on light photography and judged by a medical and nonmedical panel, was assessed after 3 days, 7 days, and 6 weeks. Secondary endpoints were swelling, ecchymosis, erythema, pain, and patient satisfaction with recovery and outcome.
Results: There was no significant difference between arnica and placebo in overall judgment of periorbital appearance 3 days, 7 days, and 6 weeks after surgery. Furthermore, swelling, ecchymosis, erythema, pain, and patient satisfaction with recovery and outcome did not differ between arnica and placebo. Postoperative outcome in untreated eyelids was not different from eyelids treated with either arnica or placebo on any of the studied outcome measures.
Conclusion: The authors' study demonstrates that topical arnica ointment after upper blepharoplasty does not improve postoperative outcome. (*Plast. Reconstr. Surg.* 138: 66, 2016.)
CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, II.

Arnica, a mountain herb also known as *Arnica montana*, is traditionally used after traumatic injuries, such as sprains and bruises. Arnica also gained popularity as a preventive measure to reduce swelling and ecchymosis following elective surgical procedures.[1] From a mechanistic point of view, it has been suggested that arnica can modulate histamine release in the vascular endothelial cell wall and affect vascular permeability.[2] Furthermore, constituents of arnica were reported to inhibit human thromboxane formation and collagen-induced platelet function.[3] However, convincing evidence of the pathophysiologic mechanism that explains the purported treatment effect of arnica has yet to be established.

Although few remedies consist of undiluted arnica, most preparations are homeopathic and rely on the assumption that systematic dilution of the arnica ground substance causes a

From the Departments of Plastic Surgery and Innovation and Science, Isala; the Department of Plastic Surgery, Diakonessenhuis Utrecht; the Department of Plastic Surgery, University of Groningen and University Medical Center Groningen; and the Bergman Clinics.
Received for publication August 28, 2015; accepted February 11, 2016.
This trial is registered under the name "Efficacy of Arnica D1 Ointment After Upper Blepharoplasty (ARINE)," ClinicalTrials.gov identification number NCT01598909 (https://clinicaltrials.gov/ct2/show/NCT01598909).
Data from this study were presented at The Netherlands Society for Plastic Surgery, in Tilburg, The Netherlands, October 4 through October 5, 2014.

DOI: 10.1097/PRS.0000000000002249

Disclosure: *Weleda AG, Germany, has provided the study medication. The authors declare that they have not had any related financial interests or commercial associations during the course of this study..*

strengthening of the opposite effect of the undiluted form. The higher the number of sequential dilutions, the stronger its potency would be.[4] Homeopathic potency scales use decimal (1:10), centesimal (1:100), or millesimal (1:1000) to indicate the diluting factor at each stage, and the number reflects the number of times this dilution is repeated (e.g., a centesimal 6 preparation implicates a $100^{-6} = 10^{-12}$ dilution factor). In high-potency homeopathic preparations, the number of sequential dilutions makes it unlikely that they contain even one molecule of the ground substance. In light of current pharmacologic understanding, this renders an observed treatment effect of any high-potency homeopathic preparation unlikely to be related to the substance itself.[5] In contrast, it should be appreciated that low-potency preparations do contain substantial amounts of the ground substance, which is irrespective of their manufacturing according to homeopathic principles.

For advocates of arnica treatment, the eyelid forms a particularly interesting area. Given the unique eyelid anatomy—it constitutes the thinnest skin of the body and, at the same time, is very well vascularized—the undesirable phenomenon of swelling and ecchymosis after blepharoplasty is common. In our 2012 case series of 416 consecutive upper blepharoplasty patients, 18 percent of patients used arnica perioperatively (unpublished data). Although a placebo-controlled trial found no efficacy of oral high-potency homeopathic arnica on the occurrence of postoperative ecchymosis after upper blepharoplasty,[6] studies on the topical use of relatively undiluted homeopathic arnica are still lacking. This prompted us to conduct a randomized, double-blind, placebo-controlled clinical trial on the efficacy of arnica ointment 10% after upper blepharoplasty.

PATIENTS AND METHODS

Study Design and Participants

A randomized, double-blind, placebo-controlled trial investigating the efficacy of arnica ointment 10% in upper blepharoplasty patients was undertaken at the Department of Plastic Surgery, Isala, Zwolle, The Netherlands. The study protocol was approved by its medical ethics committee and registered at ClinicalTrials.gov. Written informed consent was obtained from all study participants. From January 7, 2013, to January 7, 2014, 136 patients undergoing primary bilateral upper blepharoplasty were included for study participation. Exclusion criteria were (1) age younger than 18 years; (2) pregnancy; (3) use of anticoagulant medication; (4) previous eyelid surgery; (5) simultaneous additional periorbital surgical procedures; (6) intolerance for arnica, peanuts, or soya; and (7) recent use of arnica or other homeopathic or herbal medications.

Randomization, Intervention, and Follow-Up

Study participants were randomized for topical arnica ointment 10% or placebo ointment (both from Weleda AG, Arlesheim, Switzerland). Arnica ointment 10% contained 30 g of *Arnica planta tota* mother tincture per 100 g, corresponding to approximately 10 g of drug. Arnica ointment 10% is manufactured according to the German Homeopathic Pharmacopeia and is described as a decimal 1 preparation. However, because of its high dosage, arnica ointment 10% can be considered as herbal medication rather than homeopathic. Patients were stratified for smoking, using block randomization. Randomization was performed with Research Manager, a Web-based electronic case report form (Cloud9 Software, Deventer, The Netherlands), according to good clinical practice and good clinical data management practice guidelines and Title 21 Code of Federal Regulations Part 1 of U.S. Food and Drug Administration regulations. In both study arms, one periorbital area—a circular area including the upper and lower eyelid—was randomly designated as the treatment side, whereas the contralateral side served as an untreated internal control. Study participants were instructed to apply the ointment (arnica or placebo) to the treatment side only twice daily for 1 week, starting on the day of the blepharoplasty procedure, yet only after surgery.

Preoperatively, study participants completed a questionnaire assessing smoking behavior and the use of any conventional or alternative medicine. During surgery, a record was made of the amount of injected anesthetic solution on both sides, duration of operation (from injection of anesthetic solution to closure of the skin), and size of resected skin. Directly after surgery, the surgeon documented whether the need for hemostasis by means of coagulation had been similar on both blepharoplasty sides and whether an intuitive expectation was perceived as to which periorbital area would develop more ecchymosis, erythema, or swelling. Patients were reviewed by the first author (D.C.E.E.) on days 3 and 7 and week 6 after surgery for light photography of the periorbital areas and questioned assessing symptoms, patient satisfaction, and side effects of the ointment treatment.

Primary and Secondary Outcome Measures

The primary outcome measure was defined as the subjective overall outcome of the appearance of the periorbital areas as based on light photography. Secondary outcome measures were the degree of ecchymosis, erythema and swelling (assessed by light photography), pain and patient satisfaction with the ointment treatment and with surgical outcome (assessed by questionnaire on a visual analogue scale), and eyelid vertical aperture (assessed with a ruler). A medical (two plastic surgery consultants and one senior registrar; $n = 3$) and nonmedical panel (two secretaries and one librarian; $n = 3$), blinded and unrelated to the study protocol, evaluated the light photographs of study participants that had been taken on days 3 and 7 and week 6 after surgery. Panel members were instructed to indicate whether one of the two periorbital areas within one patient appeared superior to the other or appeared similar, and were asked to score separately for ecchymosis, erythema, swelling, and overall appearance. To obtain one outcome score per patient per time point of follow-up, a consensus meeting was organized to allow both panels to review and discuss patients that had not been scored uniformly by the individual panel members. As such, after unblinding trial participants to their treatment allocation, one of three outcome possibilities was generated per patient per panel: the treatment side (either arnica or placebo) was scored superiorly, the untreated side (internal control) was scored superiorly, or there was no difference between the treatment side and the untreated side. These data then allowed statistical analysis for comparing a treatment effect of arnica versus placebo.

Surgical Procedure

All upper blepharoplasty procedures were carried out according to a standardized protocol by either a plastic surgeon or senior registrar. After marking the area of redundant skin, the face was prepared and the surgical area was infiltrated with 1% lidocaine with 1:100,000 adrenaline. The skin was excised with a surgical blade, followed by resection of a 2- to 3-mm strip of orbicularis oculi muscle with scissors, without opening or damaging the orbital septum. The septum was then cauterized,[7] and hemostasis was carried out as needed. The skin was closed using a running subcuticular nylon suture (5-0 Ethilon; Ethicon, Inc., Somerville, N.J.). Immediately after surgery, all study participants cooled both eyelids with a cool water-filled glove for 15 minutes. Patients were instructed not to cool the eyelids at home. The first application of study ointment was carried out under guidance and with instructions from the first author before discharge from the hospital.

Sample Size Calculation

Sample size calculation was performed with IBM SamplePower 2.0 (IBM Corp., Armonk, N.Y.) and was based on a two-sample proportion. Alpha was set to 0.025 (Bonferroni correction for having selected both day 3 and day 7 as key time points for assessing the primary outcome measure), two-sided, and with a power of 80 percent. A difference of 25 percent between arnica and placebo was considered clinically relevant. Accounting for a 15 percent loss to follow-up, this resulted in a total of 136 patients included in the study.

Statistical Analysis

Categorical data were presented as number and percent. Continuous data were presented as mean ± SD or median (range) in the case of normal or skewed distribution, respectively. Categorical data were tested using Fisher's exact test. Continuous data were tested using Mann-Whitney U test. All analyses were performed two-tailed, with values of $p < 0.05$ considered to be statistically significant.

RESULTS

Of 136 patients that were enrolled in this study, 20 were excluded from analysis either because of surgeon failure to adhere to the study blepharoplasty procedure ($n = 11$) or patient failure to comply with the ointment application protocol ($n = 7$) or study follow-up scheme ($n = 2$) (Fig. 1). A total of 116 patients were available for analysis according to the study protocol, subdivided into 59 patients (50.9 percent) in the arnica arm and 57 patients (49.1 percent) in the placebo arm. Baseline characteristics, including sex, age, smoking behavior, and use of nonsteroidal anti-inflammatory drugs, were similar in both arms (Table 1). Surgery characteristics did not differ between arnica and placebo, except for a shorter duration of surgery in the arnica arm (Table 2). There were no adverse drug reactions throughout the course of this study.

Judgment of Periorbital Appearance, Ecchymosis, Erythema, and Swelling

The overall judgment of the appearance of the periorbital areas as assessed by both the

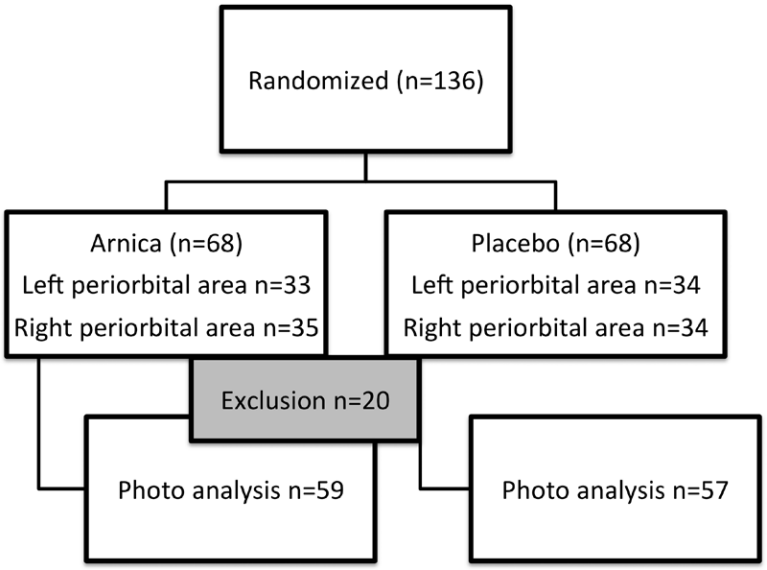

Fig. 1. Study flow diagram. Reasons for exclusion included surgeon failure to adhere to the standard blepharoplasty procedure protocol as described for this study (n = 11), patient failure to comply with the ointment application protocol (applying ointment to the contralateral eyelid; n = 3), discontinuing ointment application for several days (n = 4), or patient failure to present at follow-up (n = 2).

Table 1. Patient Characteristics after Randomization for Arnica and Placebo Treatment

Characteristic	Arnica (%)	Placebo (%)
Demographic		
No. of patients	59	57
Sex		
Women	51 (86.4)	37 (64.9)
Men	8 (13.6)	20 (35.1)
Age at the time of surgery, yr	53.6 ± 9.5	56.5 ± 8.3
Lifestyle		
Smoking		
Yes	15 (25.4)	15 (26.3)
No	44 (74.6)	42 (73.7)
Medication		
NSAIDs		
Yes	6 (10.2)	2 (3.5)
No	53 (89.8)	55 (96.5)

NSAIDs, nonsteroidal antiinflammatory drugs.

medical and nonmedical panel did not significantly differ between arnica and placebo at day 3, day 7, and week 6 after upper blepharoplasty (Table 3). Furthermore, subanalysis of ecchymosis, erythema, and swelling as secondary outcome measures showed no significant differences between arnica and placebo at any of the time points studied.

Within both the arnica arm and the placebo arm, no difference was observed between the periorbital area treated with ointment (either arnica or placebo) and its untreated (no ointment) contralateral counterpart at day 3, day 7, and week 6 after upper blepharoplasty.

Swelling

Eyelid vertical aperture, serving as a surrogate measure for the degree of postoperative swelling, was similar between arnica and placebo at all time points studied (Table 4). Moreover, application of ointment—either arnica or placebo—did not appear to affect eyelid vertical aperture compared with the untreated contralateral periorbital areas.

Postoperative Pain

Postoperative pain was similar in both arnica and placebo arms, with a visual analogue scale score of 0.1 (range, 0 to 5.6) for arnica and 0.1 (range, 0 to 2.4) for placebo (p = 0.99) on day 3, and 0 (range, 0 to 4.8) for arnica and 0.1 (range, 0 to 1) for placebo (p = 0.07) on day 7 after upper blepharoplasty.

Patient Satisfaction

Three days after surgery, 53 patients (89.8 percent) in the arnica arm reported experiencing the use of ointment as pleasant, compared with 51 patients (89.5 percent) in the placebo arm (p = 1.000). Seven days after surgery, these numbers were 52 (88.1 percent) and 52 (91.2 percent), respectively (p = 0.762). Only a small minority of

Table 2. Surgery Characteristics*

	Arnica (n = 59)				Placebo (n = 57)				
	General	Ointment Side	Contralateral Side	Difference within Patients†	General	Ointment Side	Contralateral Side	Difference within Patients†	p
Excised eyelid skin									
Length, mm		55 (range, 45–81)	57 (range, 46–80)	0 (range, –10–8)		58 ± 7.2	58.3 ± 7.2	0 (range, –10–6)	0.698
Width, mm		13.4 ± 3.5	13.5 ± 3.4	0 (range, –5–3)		14.8 ± 4.2	14.2 ± 3.7	0 (range, –4–7)	0.290
Surgery duration, min	19 (12–32)				21 (10–33)				0.025
Increased need for coagulation (yes), no. (%)‡	13 (22)				5 (8.8)				1.000
Ointment side	4 (30.8)				1 (20)				
Contralateral side	8 (61.5)				4 (80)				
Both eyes	1 (7.7)				0 (0)				
Expected symmetrical healing (yes)§	47 (82.5)				50 (84.7)				0.805

*Characteristics from surgery were similar between arnica and placebo, except for a significantly shorter duration of surgery in the arnica arm.
†Ointment side minus contralateral side: to statistically test for differences in the size of eyelid skin resections, this parameter was obtained by subtracting the size of eyelid skin resections between the ointment and contralateral side within individual patients.
‡Increased need for coagulation (yes): immediately after the surgical procedure, the operating surgeon was asked whether increased coagulation was needed to obtain hemostasis in one of the two operative sides.
§Expected symmetrical healing (yes): immediately after the surgical procedure, the operating surgeon was asked whether normal symmetrical eyelid healing was expected in light of the procedure performed.

patients reported the ointment regimen to be unpleasant on day 3 (arnica arm, 3.4 percent; placebo arm, 5.3 percent, $p = 0.677$) or day 7 (arnica arm, 1.7 percent; placebo arm, 1.8 percent; $p = 1.000$), or painful on day 3 (arnica arm, 1.7 percent; placebo arm, 0 percent; $p = 1.000$) or day 7 (arnica arm, 1.7 percent; placebo arm, 0 percent; $p = 1.000$).

Approximately half of all patients (arnica arm, 61 percent; placebo arm, 47.4 percent; $p = 0.298$) would recommend postoperative ointment application to others, whereas 22 percent in the arnica arm and 33 percent in the placebo arm ($p = 0.015$) would specifically advise against doing so. Satisfaction with postoperative recovery, assessed 6 weeks after surgery, was high in both the arnica arm [9.1 (range, 4.9–10)] and the placebo arm [9.5 (range, 7.1–10)] ($p = 0.297$). Similarly, satisfaction with the postoperative functional and cosmetic outcome was high, scoring 9.3 (range, 5.5 to 10) in the arnica arm and 9.3 (range, 3 to 10) in the placebo arm ($p = 0.872$).

DISCUSSION

This randomized, double-blind, placebo-controlled trial demonstrates that periorbital application of arnica ointment does not improve the outcome of upper blepharoplasty. Arnica did not affect periorbital appearance as assessed 3 days, 7 days, and 6 weeks after upper blepharoplasty. Furthermore, ecchymosis, erythema, swelling, pain, patient satisfaction with ointment use, patient satisfaction with postoperative recovery, and postoperative outcome were not different between eyelids treated with arnica and eyelids treated with placebo.

Arnica has a traditional role in the prevention or treatment of swelling, ecchymosis, and associated pain following traumatic or surgical injury.[8] However, a systematic review of the literature summarized that homeopathy in general and homeopathic arnica in particular has no efficacy beyond placebo.[9] The purported efficacy of arnica in the perioperative setting has been addressed in several placebo-controlled trials. Although Seeley et al. found significantly less ecchymosis in postrhytidectomy patients taking perioperative homeopathic arnica,[10] outcomes of other placebo-controlled trials have been negative; homeopathic arnica had no effect on the extent and intensity of postrhinoplasty ecchymosis[11]; the amount of postoperative pain, bruising, and swelling after elective hand surgery[12]; or on hematoma and pain after varicose vein surgery.[13] Kotlus et al.[6] demonstrated that

Table 3. Judgment of Periorbital Appearance*

	Arnica ($n = 59$)			Placebo ($n = 57$)			
	Arnica Side Better (%)	No Difference (%)	Contralateral Side Better (%)	Placebo Side Better (%)	No Difference (%)	Contralateral Side Better (%)	*p*
Day 3							
Medical panel							
Ecchymosis	17 (28.8)	20 (33.9)	22 (37.3)	15 (26.3)	25 (43.9)	17 (29.8)	0.566
Erythema	17 (28.8)	28 (47.5)	14 (23.7)	12 (21.1)	33 (57.9)	12 (21.1)	0.533
Swelling	7 (11.9)	37 (62.7)	15 (25.4)	7 (12.3)	39 (68.4)	11 (19.3)	0.724
Total	16 (27.1)	22 (37.3)	21 (35.6)	13 (22.8)	28 (49.1)	16 (28.1)	0.443
Nonmedical panel							
Ecchymosis	11 (18.6)	32 (54.2)	16 (27.1)	10 (17.5)	35 (61.4)	12 (21.1)	0.690
Erythema	10 (16.9)	36 (61)	13 (22)	10 (17.5)	36 (63.2)	11 (19.3)	0.964
Swelling	7 (11.9)	45 (76.3)	7 (11.9)	4 (7)	48 (84.2)	5 (8.8)	0.586
Total	11 (18.6)	36 (61)	12 (20.3)	10 (17.5)	37 (64.9)	10 (17.5)	0.930
Day 7							
Medical panel							
Ecchymosis	11 (18.6)	35 (59.3)	13 (22)	8 (14)	40 (70.2)	9 (15.8)	0.468
Erythema	5 (8.5)	49 (83.1)	5 (8.5)	1 (1.8)	51 (89.5)	5 (8.8)	0.303
Swelling	2 (3.4)	53 (89.8)	4 (6.8)	2 (3.5)	50 (87.7)	5 (8.8)	0.901
Total	7 (11.9)	44 (74.6)	8 (13.6)	7 (12.3)	39 (68.4)	11 (19.3)	0.699
Nonmedical panel							
Ecchymosis	10 (16.9)	39 (66.1)	10 (16.9)	8 (14)	41 (71.9)	8 (14)	0.815
Erythema	8 (13.6)	42 (71.2)	9 (15.3)	4 (7)	47 (82.5)	6 (10.5)	0.349
Swelling	2 (3.4)	56 (94.9)	1 (1.7)	1 (1.8)	54 (94.7)	2 (3.5)	0.853
Total	9 (15.3)	40 (67.8)	10 (16.9)	8 (14)	42 (73.7)	7 (12.3)	0.773
Week 6							
Medical panel							
Ecchymosis	0 (0)	58 (98.3)	1 (1.7)	0 (0)	57 (100)	0 (0)	1.000
Erythema	0 (0)	58 (98.3)	1 (1.7)	0 (0)	57 (100)	0 (0)	1.000
Swelling	0 (0)	59 (100)	0 (0)	0 (0)	57 (100)	0 (0)	NA
Total	0 (0)	58 (98.3)	1 (1.7)	0 (0)	57 (100)	0 (0)	1.000
Nonmedical panel							
Ecchymosis	0 (0)	58 (98.3)	1 (1.7)	0 (0)	57 (100)	0 (0)	1.000
Erythema	0 (0)	58 (98.3)	1 (1.7)	0 (0)	57 (100)	0 (0)	1.000
Swelling	0 (0)	59 (100)	0 (0)	0 (0)	57 (100)	0 (0)	NA
Total	0 (0)	58 (98.3)	1 (1.7)	0 (0)	57 (100)	0 (0)	1.000

NA, not applicable.
*Judgment of ecchymosis, erythema, swelling and overall periorbital appearance by the medical and nonmedical panels showed no significant differences between arnica and placebo on day 3, day 7, and week 6 after surgery.

Table 4. Eyelid Vertical Aperture*

	Arnica ($n = 59$)		Placebo ($n = 57$)	
Eyelid Vertical Aperture	Ointment Side (range) (mm)	Contralateral Side (range) (mm)	Ointment Side (range) (mm)	Contralateral Side (range) (mm)
Preoperative space	9 (6–12)	9 (6–12)	9 (5–12)	9 (5–12)
Postoperative day 3 space	8 (5–12)	8 (4–12)	8 (5–12)	8 (5–11)
Postoperative day 7 space	9 (5–12)	9 (5–12)	9 (6–12)	9 (6–12)

*Eyelid vertical aperture served as surrogate marker for the degree of postoperative swelling and was similar between arnica, placebo, and untreated eyelids.

oral homeopathic arnica did not affect the development or resolution of ecchymosis after upper blepharoplasty, which is in line with the results of our present study on topical arnica. Likewise, topical homeopathic arnica decimal 1 gel had no beneficial effect on the prevention or resolution of facial postlaser treatment bruises.[14] Despite these studies, patients and surgeons continue to use arnica regularly in daily practice.[15]

Another finding of this study is that repeated pressure to and rubbing of the surgical site, which is intrinsic in ointment application, does not worsen postoperative outcome. Indeed, untreated periorbital areas, serving as intraindividual controls in both the arnica and placebo arms, scored similarly on the degree of ecchymosis, swelling, hematoma, and overall appearance compared with the periorbital areas that had been treated with either arnica or placebo. On one hand, one would assume that keeping a recent surgical site moist by means of applying ointment provides superior healing conditions and would accelerate

healing. On the other hand, one could argue that manipulation of a recently operated surgical site (e.g., by ointment application) could cause additional swelling or hematoma and would worsen outcome. Our study demonstrates that neither of the two is the case. We speculate that these potential advantages and disadvantages of ointment application are not significant enough to overcome the extent of tissue injury that arises as a direct consequence of the surgical procedure.

Furthermore, only three patients in the arnica arm and three patients in the placebo arm reported experiencing discomfort from ointment application, although this did not prompt them to discontinue the study protocol. Considered together, these data illustrate that mechanical forces to the fresh surgical blepharoplasty site associated with ointment application seem to be insignificant in terms of outcome and patient satisfaction.

It is well known that both surgeons and patients like to impose measures to improve postoperative recovery. In cosmetic facial surgery, most attempted measures are directed to counteract the development of ecchymosis, swelling, and pain. It is remarkable that many of these measures are highly popular and widespread despite the lack of supporting scientific evidence. Examples of these habits include avoidance of bending over, heavy lifting, or straining; and excessive smiling or yawning, sleeping with the head elevated, wearing sunglasses to prevent squinting, and use of (antibiotic) ophthalmic ointment at the incision sites. Cooling of the eyelids postoperatively—another common phenomenon—was recently shown not to reduce edema, erythema, or ecchymosis of the eyelids after upper blepharoplasty, and postoperative outcome appeared to be unaffected.[16] Arnica treatment, either topically with ointment 10% as demonstrated in this study and orally as demonstrated previously,[6] can now be added to the list of ineffective postblepharoplasty measures. Although advocates of homeopathic arnica would argue that side effects are unlikely attributable to the homeopathic nature of the preparation—because of extreme dilution of the arnica ground substance—surgeons with a neutral or positive attitude toward arnica use by their patients should perhaps now reconsider its use because not all topical treatments are innocuous, and bear the risk of skin irritation, itching, and allergic eczema.[17] More seriously, ingestion of relevant doses of arnica-containing products has induced gastroenteritis, tachycardia, and muscular weakness, and has even led to death.[18] These issues of safety, which were also encountered with similar alternative or complementary remedies, prompted the American Society of Anesthesiologists to recommend that surgical patients need to stop taking any of these medicines 2 to 3 weeks before surgery.[19]

Our study has limitations. First, the comparison between arnica and placebo is based on the comparison between patients rather than within patients. This implicates that results might be affected by interindividual tendencies for the development of ecchymosis, erythema, swelling, and pain. The principal reason not to compare arnica to placebo within one patient was the likeliness of ointment contamination between the two eyelids, as study participants then could have easily and repeatedly mistaken designated ointment sides during the course of the study or used the same finger to apply both ointments. Second, for reasons of practicality, the blepharoplasty procedures were carried out by more than one surgeon, which introduces the risk of surgeon-related differences between patients. We attempted to minimize this risk by meticulously instructing surgeons with a detailed, step-by-step surgical study protocol. Moreover, surgeons had to document their adherence to the surgical protocol immediately after the procedure. We did not observe differences in surgical characteristics between the two study arms in terms of excised eyelid skin size, use of peroperative coagulation, or surgeon expectancy of symmetric healing, reflecting a certain degree of homogeneity despite the involvement of more than one surgeon. Although duration of surgery was significantly shorter in the arnica arm, the absolute difference is so small that it is unlikely to represent a clinically relevant difference. Third, patient compliance with the study protocol and specifically with regard to the importance of ointment application to only one and not both eyelids could be a matter of concern. We assessed patient compliance with the ointment protocol twice during their treatment week, yet it cannot be completely ruled out that some patients have neglected the strict instructions that were provided in both preoperative and postoperative consultations. Fourth, our protocol of applying ointment twice a day for 1 week starting directly after surgery may not have been sufficient to have a significant effect in this study. Nevertheless, our regimen does reflect its use in general practice, is in line with the information in the package leaflets of the pharmaceutical company, and is similar to the protocol of related studies investigating the efficacy of topical arnica on bruising.[14] Finally, although our observations could be applicable to

other cosmetic surgical procedures, these findings cannot be extrapolated directly as such.

CONCLUSIONS

Our study demonstrates that the use of topical arnica after upper blepharoplasty does not reduce postoperative ecchymosis, erythema, swelling, or pain of the eyelids, nor does it increase patient satisfaction with postoperative recovery or outcome. These findings should be used in clinical practice by plastic surgeons to inform blepharoplasty patients about the lack of evidence for a role of arnica in postoperative recovery.

Wyland B. W. H. Melenhorst, M.D., Ph.D.
Prof. Sproncklaan 40, 3705 AD
Zeist, The Netherlands
wmelenho@diakhuis.nl

ACKNOWLEDGMENT

The Zwols Wetenschapsfonds Isala Klinieken, Isala, Zwolle, The Netherlands, has funded this study to cover for travel costs by study participants. We thank David de Jong for electronic case report form development.

REFERENCES

1. Kouzi SA, Nuzum DS. Arnica for bruising and swelling. *Am J Health Syst Pharm.* 2007;64:2434–2443.
2. Macêdo SB, Ferreira LR, Perazzo FF, Carvalho JC. Anti-inflammatory activity of *Arnica montana 6cH*: Preclinical study in animals. *Homeopathy* 2004;93:84–87.
3. Schröder H, Lösche W, Strobach H, et al. Helenalin and 11 alpha,13-dihydrohelenalin, two constituents from *Arnica montana L.*, inhibit human platelet function via thiol-dependent pathways. *Thromb Res.* 1990;57:839–845.
4. Dekkers J. *What about Homeopathy? A Comparative Investigation into the Causes of Current Popularity of Homeopathy in the USA, The UK, India and The Netherlands* (M.A. thesis). Neunen, The Netherlands: University of Utrecht; 2009.
5. Shang A, Huwiler-Müntener K, Nartey L, et al. Are the clinical effects of homoeopathy placebo effects? Comparative study of placebo-controlled trials of homoeopathy and allopathy. *Lancet* 2005;366:726–732.
6. Kotlus BS, Heringer DM, Dryden RM. Evaluation of homeopathic *Arnica montana* for ecchymosis after upper blepharoplasty: A placebo-controlled, randomized, double-blind study. *Ophthal Plast Reconstr Surg.* 2010;26:395–397.
7. van der Lei B, Timmerman IS, Cromheecke M, Hofer SO. Bipolar coagulation-assisted orbital (BICO) septoblepharoplasty: A retrospective analysis of a new fat-saving upper-eyelid blepharoplasty technique. *Ann Plast Surg.* 2007;59:263–267.
8. Iannitti T, Morales-Medina JC, Bellavite P, Rottigni V, Palmieri B. Effectiveness and safety of *Arnica montana* in post-surgical setting, pain and inflammation. *Am J Ther.* 2016;23:e184–e197.
9. Ernst E, Pittler MH. Efficacy of homeopathic arnica: A systematic review of placebo-controlled clinical trials. *Arch Surg.* 1998;133:1187–1190.
10. Seeley BM, Denton AB, Ahn MS, Maas CS. Effect of homeopathic *Arnica montana* on bruising in face-lifts: Results of a randomized, double-blind, placebo-controlled clinical trial. *Arch Facial Plast Surg.* 2006;8:54–59.
11. Totonchi A, Guyuron B. A randomized, controlled comparison between arnica and steroids in the management of postrhinoplasty ecchymosis and edema. *Plast Reconstr Surg.* 2007;120:271–274.
12. Stevinson C, Devaraj VS, Fountain-Barber A, Hawkins S, Ernst E. Homeopathic arnica for prevention of pain and bruising: Randomized placebo-controlled trial in hand surgery. *J R Soc Med.* 2003;96:60–65.
13. Ramelet AA, Buchheim G, Lorenz P, Imfeld M. Homeopathic arnica in postoperative haematomas: A double-blind study. *Dermatology* 2000;201:347–348.
14. Alonso D, Lazarus MC, Baumann L. Effects of topical arnica gel on post-laser treatment bruises. *Dermatol Surg.* 2002;28:686–688.
15. Lawrence WT; Plastic Surgery Educational Foundation DATA Committee. Arnica. *Plast Reconstr Surg.* 2003;112:1164–1166.
16. Pool SM, van Exsel DC, Melenhorst WB, Cromheecke M, van der Lei B. The effect of eyelid cooling on pain, edema, erythema, and hematoma after upper blepharoplasty: A randomized, controlled, observer-blinded evaluation study. *Plast Reconstr Surg.* 2015;135:277e–281e.
17. Widrig R, Suter A, Saller R, Melzer J. Choosing between NSAID and arnica for topical treatment of hand osteoarthritis in a randomised, double-blind study. *Rheumatol Int.* 2007;27:585–591.
18. Final report on the safety assessment of *Arnica montana* extract and *Arnica montana*. *Int J Toxicol.* 2001;20(Suppl 2):1–11.
19. Wong WW, Gabriel A, Maxwell GP, Gupta SC. Bleeding risks of herbal, homeopathic, and dietary supplements: A hidden nightmare for plastic surgeons? *Aesthet Surg J.* 2012;32:332–346.