



The Effectiveness of Bromelain on Oedema, Subconjunctival Haemorrhage, and Ecchymosis After Rhinoplasty: A Randomised, Double-Blind, Placebo-Controlled Trial



Benyamin Rahmaty^{1,8} · Mohsen Naraghi^{2,3} · Alireza Mesbahi⁴ · Alireza Mohebbi⁵ · Bahman Sadeghi⁷ · Amir Reza Zadeh⁶ · Amir Almasi⁷

Received: 18 October 2024 / Accepted: 12 December 2024

© Springer Science+Business Media, LLC, part of Springer Nature and International Society of Aesthetic Plastic Surgery 2025

Abstract

Objective To evaluate the effectiveness of bromelain on periorbital oedema, subconjunctival haemorrhage, and ecchymosis after preservation rhinoplasty.

Study Design Randomised, double-blind, placebo-controlled trial

Setting Tertiary referral centre

Methods In this double-blind clinical trial, participants aged 18–45 who were scheduled for open preservation rhinoplasty using the push-down technique and lateral osteotomy were recruited. Twenty-three cases were assigned to the placebo group and twenty-three to the experimental group Bromelain.

Results Regarding gender, 17.39% (8 cases) were male, and 82.61% (38 cases) were female. Comparing the severity of left and right eye ecchymosis between groups at different times showed that bromelain was significantly effective on both sides on the 7th day ($p = 0.012$). Like ecchymosis, the results demonstrated that bromelain was also considerably effective on subconjunctival haemorrhage on the seventh day post-operatively ($p = 0.015$). However, the intensity of oedema between groups at different times did not significantly differ.

Conclusion Bromelain increases serum fibrinolytic activity and decreases plasma fibrinogen levels. It is significantly more effective on subconjunctival haemorrhage and ecchymosis compared with the placebo on the seventh day in both eyes after rhinoplasty. Hence, this study indicates that bromelain is remarkably more effective than a placebo in reducing subconjunctival haemorrhage and ecchymosis. **Trial registration** Iranian Registry of Clinical Trials ID: IRCT20180519039720N2

Level of Evidence I This journal requires that authors assign a level of evidence to each article. For a full description of these Evidence-Based Medicine ratings, please refer to the Table of Contents or the online Instructions to Authors www.springer.com/00266.

Keywords Bromelain · Rhinoplasty · Subconjunctival haemorrhage · Ecchymosis · Oedema

Introduction

Rhinoplasty, commonly known as a nose job, is one of the most frequent cosmetic surgeries performed in Iran, with the latest figures indicating an annual total of 37,423 procedures. This procedure is primarily performed to modify

✉ Benyamin Rahmaty
Benyamin.rahmaty@gmail.com; B-rahmaty@razi.tums.ac.ir

¹ Head and Neck Surgery Department, Arak University of Medical Sciences, Arak, Iran

² Department of Otorhinolaryngology-Head and Neck Surgery, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

³ Rhinology Research Society, Orphans Worldwide, Jacksonville, Florida, USA

⁴ Shiraz, Iran

⁵ ENT and Head and Neck Research Center and Department, School of Medicine, The Five Senses Health Institute, Iran University of Medical Sciences, Tehran, Iran

⁶ Department of Clinical Pharmacy, Iran University of Medical Sciences, Tehran, Iran

⁷ Department of Epidemiology, Student Research Committee, Arak University of Medical Sciences, Arak, Iran

⁸ Otolaryngology Research Center, Amir Alam Hospital, Tehran University of Medical Sciences, Northern Saadi Ave, District 12, Tehran, Iran

facial shape and improve respiratory function. The history of rhinoplasty dates back to between 2500 and 3000 B.C. and is related to correcting deformities resulting from nasal fractures [1]. During this long period, the rhinoplasty procedure has continuously evolved. Today, the methods of performing this surgery are divided into two general categories: open or external (Trans-Columellar) surgery and closed or endonasal surgery. In both cases, two common primary facial characteristics of rhinoplasty are periorbital oedema and ecchymosis post-operatively, which are often troublesome and undesirable in many cases [2–4].

Two primary steps of rhinoplasty, in both open and closed approaches, involve removing the hump and performing osteotomies to correct and restore a more favourable nasal bone pyramid. Lateral osteotomy is the leading cause of periorbital oedema and ecchymosis following rhinoplasty. Conversely, correcting the deviation of the nasal pyramid and modifying the nasal width is unavoidable in many instances [5–8].

Many therapies have been used to reduce periorbital oedema and ecchymosis, including steroid injections during and after the procedure, ice packs or cold pads, applying pressure on the site after osteotomy, and taping the nose [8–13]. A single dose of dexamethasone before Rhinoplasty reduces oedema and ecchymosis after the surgery [10]. The haemostatic effectiveness of desmopressin perioperatively is also noted to reduce blood loss in rhinoplasty [14].

Lidocaine and epinephrine injections in a ratio of one to one hundred thousand before performing lateral osteotomy

have also been evaluated. This combination did not reduce the amount of oedema and ecchymosis [11]. However, high-dose corticosteroids reduce the amount of periorbital oedema and ecchymosis after rhinoplasty [12]. An ice pack applied around the nose and eyes also reduces the amount of periorbital oedema and ecchymosis post-operatively [13].

However, despite the existing and recommended methods, periorbital oedema and ecchymosis are the main concerns of patients, and none of the solutions have been able to prevent these complications definitively [8, 13, 15]. Bromelain, extracted from pineapple, contains a combination of proteolytic enzymes. This supplement exhibits anti-inflammatory and analgesic effects by blocking bradykinin and regulating prostaglandin levels synthesis [15–17]. Clinical studies have demonstrated that bromelain is beneficial in alleviating bothersome symptoms across various ailments. Some therapeutic benefits of bromelain include relieving and reducing the intensity of joint pain associated with osteoarthritis, gout, menstrual discomfort, autoimmune diseases, ulcerative colitis, angina pectoris, transient ischaemic attacks, and the prevention of sports injuries [16–18].

Recently, in Iran, there has been a surge of publicity from pharmaceutical companies concerning using bromelain to reduce swelling and bruising after rhinoplasty, taking a daily dose of two to three 500 GDU-200mg capsules. This supplement is extracted from pineapple, and its mechanism of action may be attributed to the proteolytic enzymes it contains [19]. In addition, this drug has anti-

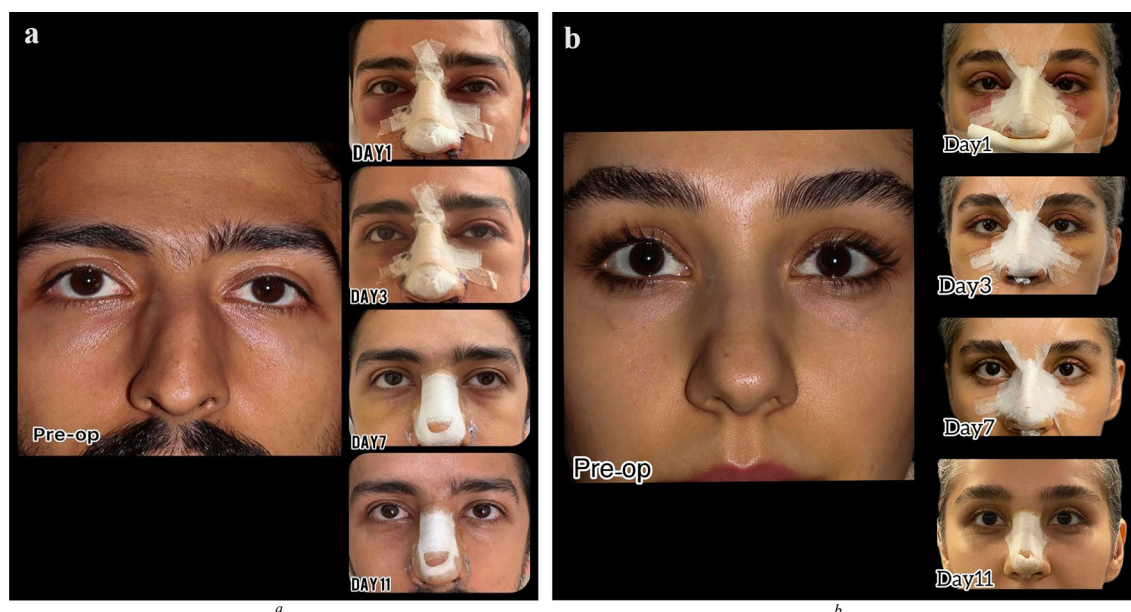


Fig. 1 **a** and **b** Present cases of patients who underwent rhinoplasty, with photographs taken at different times pre- and post-operatively (Bromelain group)

Fig. 2 a, b, and c: Show photographs taken at different times pre- and post-operatively (Placebo group)



Table 1 The baseline characteristics of the patients

Variables		Bromelain <i>n</i> = 23	Placebo <i>n</i> = 23	Total <i>n</i> = 46	<i>P</i>
Age	Mean (SD)	30.43 (10.67)	32.65 (9.61)	31.54 (10.10)	0.463
Gender	Male	3 (13.04)	5 (21.74)	8 (17.39)	0.435
	Female	20 (86.96)	18 (78.26)	38 (82.61)	
Comorbidity (none)	Does not have	23 (100)	23 (100)	46 (100)	–

inflammatory properties and reduces oedema, inflammation, and trismus after jaw and facial surgery [20, 21]. This drug has also been used for enzymatic debridement in burn wounds, and its efficacy in reducing swelling and inflammation has been noted in numerous other conditions [22–24]. Some studies have also reported a reduction in

swelling following dental procedures [25, 26]. So far, no clinical trials have been conducted to investigate the benefits of this drug following rhinoplasty. Hence, we decided to examine the effectiveness of this supplement in reducing swelling and bruising after Rhinoplasty.

Table 2 Comparison of left and right eye oedema between two groups

Side	Day	Oedema	Bromelain <i>n</i> = 23	Placebo <i>n</i> = 23	<i>P</i>
Left	1	None	1 (4.35)	2 (8.70)	0.434
		Minimal	7 (30.43)	5 (21.74)	
		Partial	7 (30.43)	8 (34.78)	
		Complete	8 (34.78)	6 (26.09)	
		Full closure	0	2 (8.70)	
	3	None	0	1 (4.35)	0.563
		Minimal	9 (39.13)	9 (39.13)	
		Partial	10 (43.48)	9 (39.13)	
		Complete	4 (17.39)	3 (13.04)	
		Full closure	0	1 (4.35)	
	7	None	13 (56.52)	15 (65.22)	0.757
		Minimal	8 (34.78)	5 (21.74)	
		Partial	1 (4.35)	2 (8.70)	
		Complete	1 (4.35)	1 (4.35)	
		Full closure	0	0	
	11	None	22 (95.65)	23 (100)	0.235
		Minimal	1 (4.35)	0	
		Partial	0	0	
		Complete	0	0	
		Full closure	0	0	
Right	1	None	1 (4.35)	1 (4.35)	0.570
		Minimal	7 (30.43)	6 (26.09)	
		Partial	8 (34.78)	8 (34.78)	
		Complete	7 (30.43)	6 (26.09)	
		Full closure	0	2 (8.70)	
	3	None	0	0	0.651
		Minimal	9 (39.13)	10 (43.48)	
		Partial	10 (43.48)	9 (39.13)	
		Complete	4 (17.39)	3 (13.04)	
		Full closure	0	1 (4.35)	
	7	None	13 (56.52)	15 (65.22)	0.757
		Minimal	8 (34.78)	5 (21.74)	
		Partial	1 (4.35)	2 (8.70)	
		Complete	1 (4.35)	1 (4.35)	
		Full closure	0	0	
	11	None	22 (95.65)	23 (100)	0.235
		Minimal	1 (4.35)	0	
		Partial	0	0	
		Complete	0	0	
		Full closure	0	0	

Methods

Trial Design

This study is registered in the Iranian Registry of Clinical Trials (IRCT) under the registration number

IRCT20180519039720N2. In this double-blind clinical trial, participants aged 18–45 who were scheduled for open preservation rhinoplasty—including lateral osteotomy, radix osteotomy, the push-down technique, and cartilage preservation as components of their surgical planning—were recruited. Participants were not permitted to take anti-inflammatory drugs or steroids during or after the surgery, and cold compresses post-surgery were also prohibited.

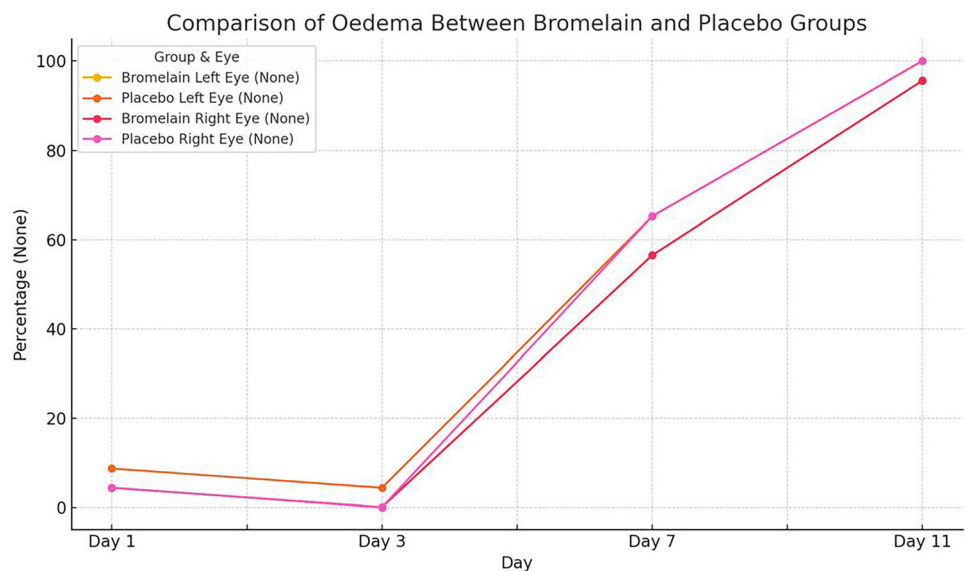
Other exclusion criteria included the absence of hypertension, coagulation disorders, and any history of allergy to bromelain or pineapple products. We did not prescribe painkillers to either group; instead, we just administered acetaminophen 500 mg every 6 hours to both groups.

After obtaining informed consent, the inclusion and exclusion criteria were reviewed. Subsequently, all participants underwent open preservation rhinoplasty- subperi-chondrial and subperiosteal approaches for flap elevation and lateral and radix osteotomies during the surgery, employing only the push-down technique for the bony dorsum. All crucial components, including the Pitanguy ligament and scroll area, were preserved and repaired during and after the procedure. We also preserved all cartilages except for the subdorsal strip to facilitate the push-down of the dorsum. Following the procedure, a group of 23 individuals was randomly assigned to receive Bromelain 200 mg capsules (equivalent to 500 GDU) every 8 h. The placebo group received starch-filled capsules, which appeared similar, every 8 h. Postoperative oedema and ecchymosis were assessed on days 1, 3, 7, and 11. These were scored from 1 to 4 based on the method developed by Mohamed Abdelwahab and P. Most study [27] by an otolaryngologist examiner who was unaware of the group assignments. At each visit, a facial photograph of each patient was also taken (Figures 1 and 2).

Randomisation Method

Two-group randomisation on the web (www.graphpad.com) created a simple random sequence. The closed envelope method and the random sequence were employed to conceal the random allocation. SNOSE utilised several envelopes and preparations, and each random sequence was recorded on a card, which was then placed inside the envelopes in order. To preserve the random sequence, the outer surface of the envelopes was numbered accordingly. Finally, the lids of the letter envelopes were glued and arranged in the boxes sequentially. Subsequently, according to the order of entry of the eligible participants into the study, one of the letter envelopes was opened, and the group of that participant was assigned as A or B. Dr Bahman Sadeghi conducted the randomisation, and patients were assigned to groups by the hospital's secretary of the Otorhinolaryngology department.

Fig. 3 Comparison of oedema between bromelain and placebo groups



The double-blind study ensured that the otolaryngologist who completed the questionnaire, the patients, and those conducting the statistical analysis remained unaware of the content of the capsules and the patients' groups (double-blind).

According to the reference number [28], the sample size was equal to 23 individuals in each group:

$$n = \frac{2 \left(z_{1-\frac{\alpha}{2}} + z_{1-\beta} \right)^2 (S_1^2 + S_2^2)}{(d)^2}$$

$$\alpha = 0.05$$

$$\beta = 0.2$$

$$S_1 = 0.67$$

$$S_2 = 0.4$$

$$D = 0.25$$

$$n_1 = n_2 = 23$$

Data Analysis Methods (Statistical Analysis)

In the SPSS 22 statistical software environment, descriptive statistics are used to describe the data, including the mean, standard deviation, frequency, frequency percentage, and median.

First, the normality of the data was checked to select the appropriate statistical test.

The demographic characteristics and other essential information in the intervention and control groups were compared based on the type of variables and their corresponding indicators (mean, percentage, median) using independent *t*-tests, chi-square tests, and the Mann-Whitney *U* test.

Results

This study included 46 patients (23 in each group) in the analysis. Regarding gender, 17.39% (8 cases) were male, and 82.61% (38 cases) were female. The mean age of the participants was 31.54 years (SD: 10.1 years). No comorbidity was observed in any of the patients participating in the study. The details of the patient's baseline characteristics are shown in Table 1, separating the two groups.

Table 2 and Fig. 3 compare the intensity of left and right eye oedema in the two groups at different times. No significant difference was observed in the severity of oedema between the two groups, and the results for the left and right eyes were nearly similar.

Table 3 and Fig. 4 compare the severity of left and right eye ecchymosis between two groups at different times. The results of this table showed the significant effectiveness of Bromelain in comparison with placebo on the seventh day on both sides ($p = 0.012$). At other times, the results favoured the bromelain group but were not statistically significant.

In Table 4 and Fig. 5, compare the severity of subconjunctival haemorrhage in the left and right eyes has been compared between the two groups at different times. Similar to ecchymosis, the results of this table showed the significant effectiveness of Bromelain in comparison with placebo on the seventh day in both eyes ($p = 0.015$). At other times, the results favoured the bromelain group but were not statistically significant.

None of the patients in either group experienced any gastrointestinal symptoms, and the Bromelain group reported no side effects.

Table 3 Comparison of left and right eye ecchymosis between two groups

Side	Day	Ecchymosis (quadrants)	Bromelain <i>n</i> = 23	Placebo <i>n</i> = 23	<i>P</i>
Left	1	None	3 (13.04)	3 (13.04)	0.258
		< 1/4	2 (8.70)	5 (21.74)	
		1/4–1/2	5 (21.74)	5 (21.74)	
		1/2–3/4	9 (39.13)	3 (13.04)	
		> 3/4	4 (17.39)	7 (30.43)	
	3	None	5 (21.74)	4 (17.39)	0.414
		< 1/4	6 (26.09)	3 (13.04)	
		1/4–1/2	8 (34.78)	7 (30.43)	
		1/2–3/4	4 (17.39)	8 (34.78)	
		> 3/4	0	1 (4.35)	
	7	None	17 (73.91)	8 (34.78)	0.012
		< 1/4	2 (8.70)	10 (43.48)	
		1/4–1/2	3 (13.04)	5 (21.74)	
		1/2–3/4	1 (4.35)	0	
		> 3/4	0	0	
	11	None	22 (95.65)	20 (86.96)	0.285
		< 1/4	1 (4.35)	3 (13.04)	
		1/4–1/2	0	0	
		1/2–3/4	0	0	
		> 3/4	0	0	
Right	1	None	3 (13.04)	3 (13.04)	0.665
		< 1/4	2 (8.70)	3 (13.04)	
		1/4–1/2	6 (26.09)	6 (26.09)	
		1/2–3/4	8 (34.78)	4 (17.39)	
		> 3/4	4 (17.39)	7 (30.43)	
	3	None	5 (21.74)	4 (17.39)	0.228
		< 1/4	6 (26.09)	2 (8.70)	
		1/4–1/2	8 (34.78)	7 (30.43)	
		1/2–3/4	4 (17.39)	9 (39.13)	
		> 3/4	0	1 (4.35)	
	7	None	17 (73.91)	8 (34.78)	0.012
		< 1/4	2 (8.70)	10 (43.48)	
		1/4–1/2	3 (13.04)	5 (21.74)	
		1/2–3/4	1 (4.35)	0	
		> 3/4	0	0	
	11	None	22 (95.65)	20 (86.96)	0.285
		< 1/4	1 (4.35)	3 (13.04)	
		1/4–1/2	0	0	
		1/2–3/4	0	0	
		> 3/4	0	0	

Discussion

Several steps exist to increase patient comfort before, during, and after rhinoplasty. These steps may vary from techniques employed while a surgeon performs this

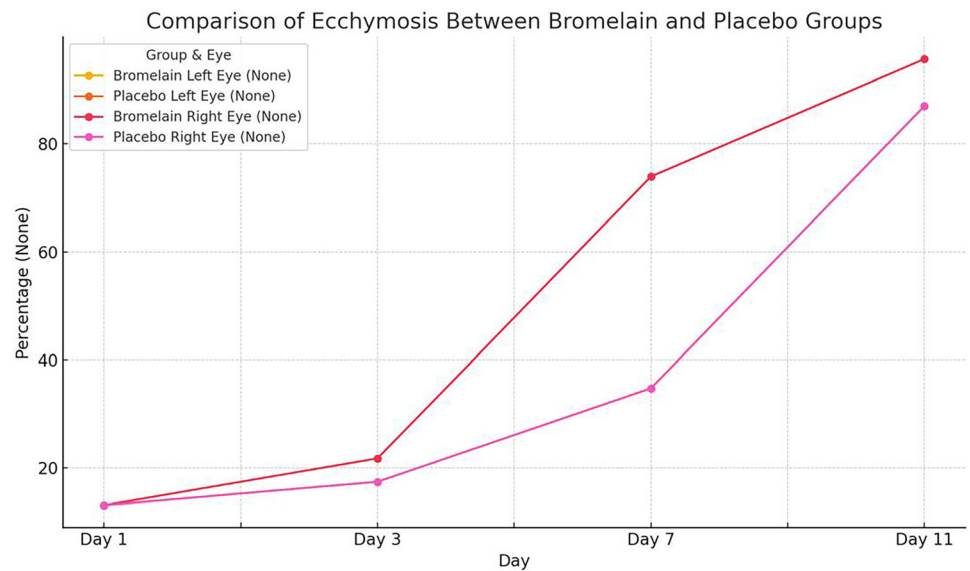
procedure to the use of supplements or medications pre-, peri-, or post-operatively [29, 30]. The main results of this trial study showed that although Bromelain does not significantly reduce oedema, it significantly affects ecchymosis and subconjunctival haemorrhage on the seventh day. The difference was clinically evident on other days but was not statistically significant.

The main therapeutic effects of bromelain are related to its proteolytic properties. Studies have shown that oral bromelain, in a dose-dependent manner, reduces the levels of bradykinin, the plasma kinin-forming system, prostaglandin E2, and thromboxane B2 in inflamed sites [18, 31–35]. Bradykinin may be the factor most responsible for pain resulting from tissue damage [18]. The advantage of bromelain over anti-inflammatory drugs is that, apart from the gastrointestinal and haemorrhagic side effects associated with non-steroidal anti-inflammatory drugs, it reduces the levels of pro-inflammatory and anti-inflammatory prostaglandins by inhibiting cyclooxygenase (COX), also known as prostaglandin-endoperoxide synthase. In contrast, bromelain selectively inhibits the production of inflammatory thromboxane and the thromboxane ratio. It shifts prostacyclin in favour of anti-inflammatory prostacyclin. Therefore, bromelain presumably reduces pain by decreasing inflammatory mediators and prostaglandins at the sites of inflammation [18].

Bromelain minimises the levels of prostaglandin E2 and thromboxane (TXA2). It also activates the collagenase enzyme, preventing abnormal and deformed collagen formation and hydrolysis in the tissue. Bromelain selectively inhibits only the biosynthesis of prostaglandins that promote inflammation. Unlike other NSAIDs, this drug does not prevent the production of prostaglandins that possess anti-inflammatory effects. Bromelain exhibits anti-inflammatory, antithrombotic, and fibrinolytic properties. It increases serum fibrinolytic activity and decreases plasma fibrin [18].

In a study conducted by Edmondson et al. [19] in 2018, a bromelain-based agent (Debrase/Debridase) played an influential role in the treatment of burn wounds and post-operative care, particularly in wounds containing necrotic tissue, where proteolytic enzymes have been used locally.

In a study conducted in 2014 [20], Bromelain was used to reduce the pain and swelling associated with latent third molar surgery, and its effect was compared with that of a pain reliever. Three parameters—pain, oedema, and erythema—were evaluated. Postoperative pain, oedema, and erythema were significantly lower in the bromelain group than in the control group. The consumption of painkillers, both in terms of the duration of treatment and the number of tablets consumed, was slightly lower in the intervention group. The authors concluded that bromelain demonstrates a critical anti-inflammatory and anti-oedema

Fig. 4 Comparison of ecchymosis between bromelain and placebo groups**Table 4** Comparison of left and right eye subconjunctival haemorrhage between two groups

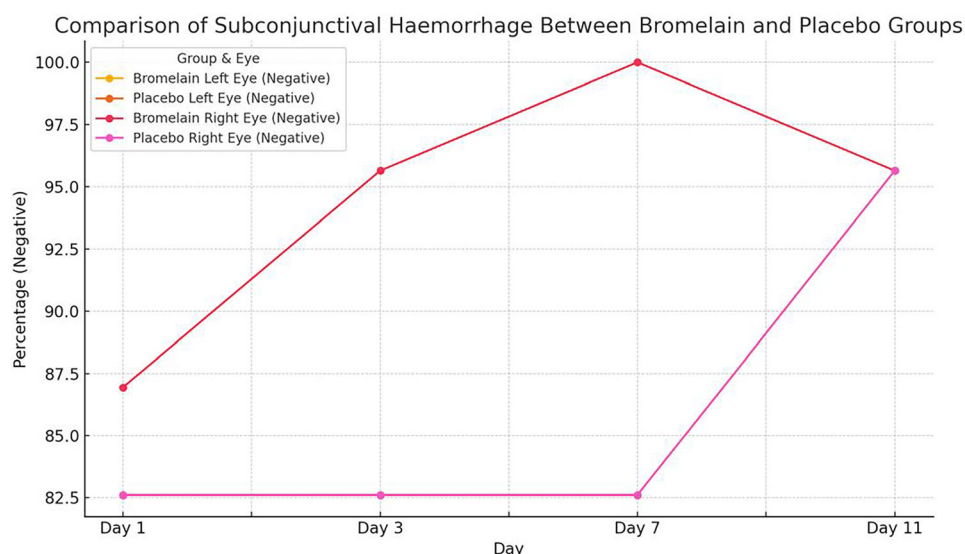
Side	Day	Subconjunctival haemorrhage	Bromelain <i>n</i> = 23	Placebo <i>n</i> = 23	<i>P</i>
Left	1	Negative	20 (86.96)	19 (82.61)	0.494
		Grade 1	3 (13.04)	3 (13.04)	
		Grade 2	0	1 (4.35)	
	3	Negative	22 (95.65)	19 (82.61)	0.143
		Grade 1	1 (4.35)	4 (17.39)	
		Grade 2	0	0	
	7	Negative	23 (100)	19 (82.61)	0.015
		Grade 1	0	4 (17.39)	
		Grade 2	0	0	
	11	Negative	22 (95.65)	22 (95.65)	0.999
		Grade 1	1 (4.35)	1 (4.35)	
		Grade 2	0	0	
Right	1	Negative	20 (86.96)	19 (82.61)	0.494
		Grade 1	3 (13.04)	3 (13.04)	
		Grade 2	0	1 (4.35)	
	3	Negative	22 (95.65)	19 (82.61)	0.143
		Grade 1	1 (4.35)	4 (17.39)	
		Grade 2	0	0	
	7	Negative	23 (100)	19 (82.61)	0.015
		Grade 1	0	4 (17.39)	
		Grade 2	0	0	
	11	Negative	22 (95.65)	22 (95.65)	0.999
		Grade 1	1 (4.35)	1 (4.35)	
		Grade 2	0	0	

effect. Following the administration of bromelain, the inflammatory response is significantly less than that of the control group. Although modalities such as ultrasound can be utilised to evaluate oedema and ecchymosis [36], in our

study, an otolaryngologist utterly blinded to the group assignments evaluated these presentations.

In 1962, Seltzer [37] evaluated bromelain in a controlled study. The effect of bromelain on the duration of

Fig. 5 Comparison of subconjunctival haemorrhage between bromelain and placebo groups



ecchymosis was assessed. Bromelain reduced the duration of ecchymosis after two days compared with the placebo. In contrast, Shehadi [38] did not find a significant difference between bromelain and placebo in reducing oedema or ecchymosis. Although these precious studies evaluated this supplement approximately fifty years ago, and we also have observed numerous changes in rhinoplasty techniques in recent years [30], the novelty of our research lies in the fact that all cases underwent preservation rhinoplasty, employing only the push-down technique for the bony dorsum and subperichondrial and subperiosteal approaches for flap elevation. We also considered all new methods to minimise trauma during the operation. We abstained from using any non-steroidal anti-inflammatory drugs (NSAIDs), steroids, or cold compresses to minimise biases. Therefore, this randomised, double-blind study evaluated the effectiveness of bromelain versus a similar appearance placebo on oedema, subconjunctival haemorrhage, and ecchymosis following the preservation rhinoplasty with minimal biases.

This research was one of the few studies to investigate the effect of bromelain in treating oedema, ecchymosis, and subconjunctival haemorrhage after rhinoplasty. Despite our promising results and the advantage of experiencing no side effects were observed compared to NSAIDs, as in some studies-Lee, Grose [39]. However, the side effect profile of Bromelain should be directly compared with NSAIDs in future studies. We also recommend further multicentre studies conducted on larger groups of patients to confirm our findings.

Conclusion

Rhinoplasty is one of the most common cosmetic surgeries performed in Iran. A leading cause of periorbital oedema and ecchymosis following rhinoplasty is lateral osteotomy. Bromelain has been shown to increase serum fibrinolytic activity and decrease plasma fibrinogen levels. This study indicates that bromelain is significantly more effective than a placebo in reducing subconjunctival haemorrhage and ecchymosis, particularly on the seventh day after the preservation rhinoplasty in both eyes. It has no reported side effects. However, our preliminary findings require further validation through more extensive studies.

Author Contributions The conception and design of the work: Benjamin Rahmaty. The conduct of the experiment, data analysis, and interpretation: Benjamin Rahmaty, Amir Reza Zadeh, and Amir Almasi. Revising the work critically for important intellectual content: Mohsen Naraghi, Alireza Mesbahi, Alireza Mohebbi, and Benjamin Rahmaty. Writing: Benjamin Rahmaty.

Funding Student Research Committee, Arak University of Medical Sciences; Grant No: 97-01-48-37203.

Declarations

Conflict of interest All co-authors have no conflict of interest to declare. We certify that no party having a direct interest in the research results supporting this article has or will benefit us or any organisation we are associated with.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical

standards. The local research ethics committee approved the present study with a reference number (IR.ARAKMU.REC.1401.243).

References

- Shiffman MA, Di Giuseppe A. *Cosmetic surgery: art and techniques*. Berlin: Springer-Verlag. 2013.
- Kargi E, Hoşnüter M, Babuççu O, Altunkaya H, Altinyazar C. Effect of steroids on edema, ecchymosis, and intraoperative bleeding in rhinoplasty. *Ann Plast Surg*. 2003;51(6):570–4.
- Hoffmann DF, Cook TA, Quatela VC, Wang TD, Brownrigg PJ, Brummett RE. Steroids and rhinoplasty. A double-blind study. *Arch Otolaryngol Head Neck Surg*. 1991;117(9):990–3.
- Kara CO, Gökalan I. Effects of single-dose steroid usage on edema, ecchymosis, and intraoperative bleeding in rhinoplasty. *Plast Reconstr Surg*. 1999;104(7):2213–8.
- Thomas JR, Griner NR, Remmler DJ. Steps for a safer method of osteotomies in rhinoplasty. *Laryngoscope*. 1987;97(6):746–7.
- Giacomarra V, Russolo M, Arnez ZM, Tirelli G. External osteotomy in rhinoplasty. *Laryngoscope*. 2001;111(3):433–8.
- Gryskiewicz JM, Gryskiewicz KM. Nasal osteotomies: a clinical comparison of the perforating methods versus the continuous technique. *Plast Reconstr Surg*. 2004;113(5):1445–56.
- Huizing, EHDG, John AM. *Functional reconstructive nasal surgery*. 2nd ed. 2015.
- M, P. *Current therapy in otolaryngology- head and neck surgery*. 6th ed. USA; Mosby. 529 1998.
- Saadallah FSA, Alzacko M, Mohammed A, Al-Khayat N. The effects of single dose dexamethasone on periorbital oedema and ecchymosis after rhinoplasty. 2010.
- Zojajy M, Alani N, Abdi Soofi S, Akbari-Dilmaghani N. Does injection of lidocaine with 1/100000 epinephrine immediately before lateral osteotomy reduce post-operative periorbital edema and ecchymosis in rhinoplasty? *Novelty Biomed*. 2014;2(2):59–63.
- Gutierrez S, Wuesthoff C. Testing the effects of long-acting steroids in edema and ecchymosis after closed rhinoplasty. *Plast Surg (Oakv)*. 2014;22(2):83–7.
- Kayiran O, Calli C. The effect of periorbital cooling on pain, edema and ecchymosis after rhinoplasty: a randomized, controlled, observer-blinded study. *Rhinology*. 2016;54(1):32–7.
- Gruber RP, Zeidler KR, Berkowitz RL. Desmopressin as a hemostatic agent to provide a dry intraoperative field in rhinoplasty. *Plast Reconstr Surg*. 2015;135(5):1337–40.
- Rohrich RJ, Janis JE, Adams WP, Krueger JK. An update on the lateral nasal osteotomy in rhinoplasty: an anatomic endoscopic comparison of the external versus the internal approach. *Plast Reconstr Surg*. 2003;111(7):2461–2.
- Meymaneh Jahromi A, Nour Elahian M, Seyedi M, Salehi M, Afzal Aghaei M. Comparison between external and internal lateral osteotomy regarding postoperative edema and ecchymosis in rhinoplasty. *Iranian J Otorhinolaryngol*. 2006;18(2):73–9.
- Locci C, Chicconi E, Antonucci R. Current uses of bromelain in children: a narrative review. *Children*. 2024;11(3):377.
- Kerkhoffs GM, Struijs PA, de Wit C, Rahlfs VW, Zwipp H, van Dijk CN. A double blind, randomised, parallel group study on the efficacy and safety of treating acute lateral ankle sprain with oral hydrolytic enzymes. *Br J Sports Med*. 2004;38(4):431–5.
- Edmondson SJ, Ali Jumabhoy I, Murray A. Time to start putting down the knife: a systematic review of burns excision tools of randomised and non-randomised trials. *Burns*. 2018;44(7):1721–37.
- de Souza GM, Fernandes IA, Dos Santos CRR, Falci SGM. Is bromelain effective in controlling the inflammatory parameters of pain, edema, and trismus after lower third molar surgery? A systematic review and meta-analysis. *Phytother Res*. 2019;33(3):473–81.
- Griffin AS, Cabot P, Wallwork B, Panizza B. Alternative therapies for chronic rhinosinusitis: a review. *Ear Nose Throat J*. 2018;97(3):E25–e33.
- Rosenberg L, Krieger Y, Bogdanov-Berezovski A, Silberstein E, Shoham Y, Singer AJ. A novel rapid and selective enzymatic debridement agent for burn wound management: a multi-center RCT. *Burns*. 2014;40(3):466–74.
- Hirche C, Citterio A, Hoeksema H, Koller J, Lehner M, Martinez JR, Monstrey S, Murray A, Plock JA, Sander F, Schulz A, Ziegler B, Kneser U. Eschar removal by bromelain based enzymatic debridement (Nexobrid®) in burns: an European consensus. *Burns*. 2017;43(8):1640–53.
- Rossella E, Giulio M, Michele M. Burns: classification and treatment. In: Maruccia M, Giudice G, editors. *Textbook of plastic and reconstructive surgery: basic principles and new perspectives*. Cham: Springer International Publishing; 2022.
- Jančić U, Gorgieva S. Bromelain and Nisin: the natural antimicrobials with high potential in biomedicine. *Pharmaceutics*. 2022;14(1):76.
- Ordesi P, Pisoni L, Nannei P, Macchi M, Borloni R, Siervo S. Therapeutic efficacy of bromelain in impacted third molar surgery: a randomized controlled clinical study. *Quintessence Int*. 2014;45(8):679–84.
- El-Sisi H, Abdelwahab M, Most SP. Association of periosteal sweeping vs periosteal preservation with early periorbital sequelae among patients undergoing external perforating osteotomy during rhinoplasty. *JAMA Facial Plastic Surgery*. 2019; 21(3):185–190.
- Jalali M, Moosavi S, Fatemi S, Banan R. Comparison between dexamethasone and tranexamic acid on postoperative edema and ecchymosis after rhinoplasty operation. *Guilan Univ Med Sci*. 2012;21:72–7.
- Ong AA, Farhood Z, Kyle AR, Patel KG. Interventions to decrease postoperative edema and ecchymosis after rhinoplasty: a systematic review of the literature. *Plast Reconstr Surg*. 2016;137(5):1448–62.
- Daniel RK, Kosins AM. Current trends in preservation rhinoplasty. *Aesthet Surg J Open Forum*. 2020;2(1):ojaa003.
- Pavan R, Jain S, Shraddha, Kumar A. Properties and therapeutic application of bromelain: a review. *Biotechnol Res Int*. 2012;2012: 976203.
- Majid OW, Al-Mashhadani BA. Perioperative bromelain reduces pain and swelling and improves quality of life measures after mandibular third molar surgery: a randomized, double-blind, placebo-controlled clinical trial. *J Oral Maxillofac Surg*. 2014;72(6):1043–8.
- Nazari Dashlibrun Y, Ramezani M, Ebrahimi Saravi M, Arabi M. Comparing the efficacy of celecoxib, ibuprofen and acetaminophen codeine in pain relief after impacted lower third molar surgery. *J Mazandaran Univ Med Sci*. 2015;24(121):94–102.
- Merry AF, Gibbs RD, Edwards J, Ting GS, Frampton C, Davies E, Anderson BJ. Combined acetaminophen and ibuprofen for pain relief after oral surgery in adults: a randomized controlled trial. *Br J Anaesthesia*. 2010;104(1):80–8. <https://doi.org/10.1093/bja/aep338>.
- Golezar S. Ananas comosus Effect on Perineal Pain and wound healing after episiotomy: a randomized double-blind placebo-controlled clinical trial. *Iran Red Crescent Med J*. 2016;18(3): e21019.
- Levin M, Ziai H, Roskies M. Modalities of post-rhinoplasty edema and ecchymosis measurement: a systematic review. *Plast Surg (Oakv)*. 2022;30(2):164–74.

37. Seltzer AP. Minimizing post-operative edema and ecchymoses by the use of an oral enzyme preparation (bromelain). A controlled study of 53 rhinoplasty cases. *Eye Ear Nose Throat Mon.* 1962;41:813–7.
38. Shehadi SI. Reducing the eyelid edema and ecchymosis that occur after corrective rhinoplasty. *Plast Reconstr Surg.* 1972;49(5):508–12.
39. Lee DJ, Grose E, Brenna CTA, Philteos J, Lightfoot D, Kirubalingam K, Chan Y, Palmer JN, Adappa ND, Lee JM. The benefits and risks of non-steroidal anti-inflammatory drugs for postoperative analgesia in sinonasal surgery: a systematic review and meta-analysis. *Int Forum Allergy Rhinol.* 2023;13(9):1738–57.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Springer Nature or its licensor (e.g. a society or other partner) holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.