Testing the effects of long-acting steroids in edema and ecchymosis after closed rhinoplasty

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BACKGROUND: Steroids have proven to be of some benefit in rhinoplasty edema and ecchymosis when administered at a high and repeated dose.

OBJECTIVE: To evaluate the effects of single-dose, long-acting intramuscular steroids on postoperative edema and ecchymosis after closed rhinoplasty with osteotomies compared with placebo.

METHODS: A randomized, double-blinded, placebo-controlled trial was performed. Fifty-four patients were randomly assigned to two groups: 28 received a single dose of long-acting dexamethasone (mean $\pm$ SD) dose 16 ± 4 mg) immediately before anesthetic induction; the remaining 26 received an intramuscular injection of saline solution. The same surgeon performed all surgeries, with patients under general anesthesia. Acetaminophen was the only analgesic used to control postoperative pain. High-resolution digital photographs were taken on postoperative days 1, 3, 7 and 14. Scoring was performed separately for eyelid swelling and ecchymosis by an independent observer using a graded scale (0 to 5) for edema and a scoring system (0 to 13) for ecchymosis.

RESULTS: No statistically significant differences in terms of age, sex or amount of bleeding during surgery were found between the two groups. No statistically significant difference was observed in the decrease of both ecchymosis and edema between placebo and high-dose, long-acting dexamethasone. A statistically significant difference in operation time was found, favouring the steroid group. No severe complications were observed due to steroid use.

DISCUSSION: Osteotomies are basically a form of (controlled) trauma, with considerable disruption of the abundant blood vessels in this facial region and, therefore, are associated with undesirable effects. A recent meta-analysis failed to show benefits of the use of steroids after postoperative day 3. Only a trend toward reduction in edema and ecchymosis with the use of long-acting steroids compared with placebo was demonstrated in the present study.

CONCLUSION: There was no benefit in administering single-dose, long-acting steroids in patients undergoing closed rhinoplasty with osteotomies.

Key Words: Edema; Ecchymosis; Rhinoplasty; Steroids

Rhinoplasty is a common procedure for both functional and cosmetic purposes. In fact, the American Society of Plastic Surgery ranked it the sixth most common elective procedure for aesthetic plastic surgery in 2009 (1). However, it can be associated with significant postoperative periorbital edema and ecchymosis caused by manipulation and trauma of the soft and hard tissues of the nasal and paranasal regions. Postoperative periorbital edema and ecchymosis remains a concern, even for the most experienced surgeons (2). The surgery's sequelae can cause social and work-related inconveniences that often result in an elevated level of patient anxiety (3), and for potential candidates, these sequelae may even represent a reason to dismiss it. Furthermore, in addition to the discomforts associated with excessive edema, such as obstructed vision and nasal blockage, it can also lead to an undesired torpid healing process of the tissues involved, while ecchymosis may lead to permanent, undesired pigmentation of the skin (2,4,5).

La vérification des effets des stéroïdes de longue durée sur l'œdème et les ecchymoses après une rhinoplastie fermée

HISTORIQUE : Il est démontré que les stéroïdes ont un certain effet positif sur l'œdème et les ecchymoses causés par la rhinoplastie lorsqu'ils sont administrés à des doses élevées et répétées.

OBJECTIF : Évaluer les effets d'une seule dose de stéroïdes intramusculaires de longue durée sur l'œdème et les ecchymoses postopératoires comparativement à un placebo après une rhinoplastie fermée avec ostéotomie.

MÉTHODOLOGIE : Les chercheurs ont mené un essai aléatoire à double insu contrôlé contre placebo. Cinquante-quatre patients ont été répartis aléatoirement en deux groupes : 28 ont reçu une dose unique de dexaméthasone de longue durée (dose moyenne $\pm$ ÉT) de 16 ± 4 mg) immédiatement avant l'induction anesthésique, et les 26 autres ont reçu une injection intramusculaire de soluté physiologique. Le même chirurgien a effectué toutes les interventions, sur des patients sous anesthésie générale. L'acétaminophène était le seul analgésique utilisé pour contrôler la douleur postopératoire. Des photographies numériques à haute résolution ont été prises les jours postopératoires 1, 3, 7 et 14. Un observateur indépendant a compilé les résultats séparément pour l'enflure des paupières et les ecchymoses au moyen d'une échelle graduée (de 0 à 5) pour l'œdème et d'un système de pointage (de 0 à 13) pour les ecchymoses.

RÉSULTATS : Les deux groupes ne présentaient pas de différence statistiquement significative en matière d'âge, de sexe ou d'abondance de sang pendant la chirurgie, ni de diminution des ecchymoses et de l'œdème entre un placebo et une forte dose de dexaméthasone de longue durée. Une différence statistiquement significative de la durée opératoire a été observée en faveur du groupe prenant des stéroïdes. Aucune grave complication n'a découlé de l'usage des stéroïdes.

EXPOSÉ : Fondamentalement, les ostéotomies sont une forme de traumatisme (contrôlé), qui perturbent énormément les vaisseaux sanguins abondants de cette région faciale. Par conséquent, elles s'associent à des effets indésirables. Une récente méta-analyse n'a pas démontré les avantages des stéroïdes après le troisième jour postopératoire. La présente étude a seulement démontré une tendance vers la réduction de l'œdème et des ecchymoses avec l'usage de stéroïdes de longue durée comparativement au placebo.

CONCLUSION : Il n'y avait pas d'avantages à administrer une dose unique de stéroïdes de longue durée aux patients subissant une rhinoplastie fermée avec ostéotomie.

Goldman et al (6) were the first to publish an article advocating the use of steroids in an attempt to manage the undesired side effects of rhinoplasty. In 1976, Kittel and Massing (7) presented their experience with 796 cases of rhinoplasty that demonstrated a "remarkable reduction" in edema after the administration of corticoid crystalline suspension in each nostril immediately after surgery. In 1989, Griffies et al (3) presented the first prospective randomized controlled trial and, since then, the topic continues to attract interest. Different regimens and types of steroids have been implemented, including dexamethasone, prednisolone, betamethasone and methylprednisolone.

Later studies found greater benefits implementing higher doses and with repeated administration after surgery. Kara and Gokalan (5) demonstrated that although beneficial, the effects of single-dose dexamethasone may be lost after the first two days, regardless of whether the dose was administered before or after surgery. This result was similar to those presented by Odzel et al (8) suggesting improvement after

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TABLE 1
Studies that favoured the use of steroids

Author (reference), year	Study design	n	Steroid used	Drug regimen	POD evaluated	Results	Other results	Cx
Koc et al (11), 2011	Prospective, randomized controlled trial	40	Methylprednisolone	Three groups: group 1) single preoperative dose of methylprednisolone; group 2) single higher preoperative dose; group 3) control group	1, 3, 7	A statistically significant difference was observed when comparing groups 1 and 2 to control group. No difference between the first two was observed	No significant difference between groups in terms of bleeding	None
Gürlek et al (10), 2009	Double-blinded, randomized trial with placebo control	40	Methylprednisolone	Five groups, with increasing doses both in frequency and mg versus one placebo group	1, 3, 7	Clinically and statistically significant difference was observed in the decrease of both ecchymosis and edema, between the placebo and high-dose methylprednisolone groups	Correlation between CRP and edema and ecchymosis	None
Gürlek et al (2), 2006	Double-blinded, randomized trial with placebo control and tenoxicam (anti-inflammatory)	40	Betamethasone Dexamethasone Methylprednisolone	Repeated doses (mg) of dexamethasone, equivalent doses of the other steroids	1, 3, 7	No differences in the levels of ecchymosis or edema among the steroid groups, the tenoxicam group and the control groups were observed	None	None
Kargi et al (9), 2003	Double-blinded, randomized study with placebo control	60	Dexamethasone	Six groups with different number of 8 mg doses, before and after surgery or both, one control (placebo) group	2, 5, 7, 10	No significant difference was observed in groups 1 and 2 (single dose 1 h and immediately after surgery respectively). On day 5, significant differences were observed in groups with preoperative dose, as well as postoperative repeated doses	No significant difference between groups in terms of bleeding	None
Kara and Gokalan (5), 1999	Double-blinded, randomized trial with placebo control	55	Dexamethasone	Three groups; group 1) 10 mg preoperatively; group 2) 10 mg postoperatively; group 3) placebo	1-9	Statistically significant difference in decreased upper eyelid ecchymosis for both the preoperative and postoperative steroid groups compared with the placebo group on the first two postoperative days	No statistically significant difference among these groups for intraoperative blood loss	None

CRP C-reactive protein; Cx Complications; POD Postoperative day

a single 10 mg dexamethasone dose after surgery during the first days. Kargi et al (9) compared the use of an 8 mg single dose of dexamethasone 1 h before surgery, immediately before surgery and with additional postoperative doses. The triple-dose groups had better results up until days 5 to 7. Gürlek et al (2) advocated the use of longer regimens, extending the administration of steroids to three days after surgery and implemented methylprednisolone as the ideal steroid if given at higher doses (10). Table 1 summarizes the studies that favoured the use of steroids.

Despite these results, such as those presented by Gürlek et al (2,10), a recent meta-analysis failed to validate the relevance of steroids past postoperative day 3 (12). Although no complications have been reported in different series (1,2,4,5,7,9-11,13-15), it is our opinion that we should consider the side effects that high doses of methylprednisolone could have if used frequently in our practice.

Other types of measures, either alone or in conjunction with steroids, have been used in an attempt to reduce these sequelae, such as arnica (15), controlled hypotension during surgery (16) and cold saline gauze compression throughout surgery (14), among others.

After a thorough review of the literature, a couple of paradigms emerge. First, the anti-inflammatory and antiechymotic effects (if any) of steroids are more effectively achieved if they are administered before performing osteotomy as opposed to after surgery. Second, the

beneficial effects of steroids are magnified if the administration is extended after the surgery (1,2,10).

Based on the latter two precepts, the principal objective of the present study was to investigate the effects of a single-dose medication that combines short- and long-acting steroids administered minutes before the beginning of surgery on periorbital edema and ecchymosis in patients who underwent closed rhinoplasty with osteotomy by the same surgeon.

METHODS

A total of 54 consecutive female patients who underwent closed rhinoplasty between February of 2010 and August 2012 were included in the present study. The Surgery Review Board and the Ethics Committee of the San Ignacio University Hospital in Bogotá, Colombia, approved the protocol. Written informed consent was obtained from all patients before any study-related activity. Exclusion criteria included peptic ulcer disease, hypertension, diabetes mellitus, psychiatric conditions and allergy to steroids. The patients, physicians, observers and outcome assessors were blinded.

Randomization

Patients were randomly assigned, on a 1:1 basis, to two groups in a blinded fashion. To accomplish this, the operating room's scrub nurse received a set of sealed envelopes, one-half of which contained a written

Figure 1) Edema classification: 0 = No edema; 1 = Minimal; 2 = Covers the iris; 3 = Covers the pupil; 4 = Difficulty opening eye, massive edema

order to administer a single dose of steroid, and the other half an order for placebo administration with saline solution. Both medications were to be administered intramuscularly before the beginning of anesthetic induction. The date and reason for opening a sealed envelope was documented, and a detailed list of all patients involved was kept by the nursing staff as well as a record of the group to which they were assigned.

Standardization was achieved by selecting female patients with similar nasal deformities (mild to moderate dorsal hump and mild to moderate laterorrhinia) only, and through the exclusion of all revisional procedures. All operations were performed via a closed approach under general anesthesia with the same surgical instruments and by the same surgeon (SG). For patients in whom placebo was administered, the anesthetist was instructed to administer a single dose of ondansetron to compensate for the lack of antiemetic effect provided by the steroids to avoid heaving that may cause further edema and ecchymosis. The same two anesthetists participated in all cases; they achieved controlled hypotension with a mean arterial blood pressure <65 mmHg in all surgeries via inhaled sevoflurane and a remifentanyl infusion.

A single dose of a combination of short- and long-acting glucocorticosteroid dexamethasone composed of 4 mg of dexamethasone sodium phosphate and 16 mg of dexamethasone acetate (Duo-Decadron, Tecnoquimicas, Colombia) was administered intramuscularly after anesthetic induction and before the first incision in patients who were randomly selected for the intervention.

The procedures began with infiltration of 1:100,000 epinephrine solution, excessive dorsal hump then was corrected in most cases through the use of a nasal rasp and, in some cases, by hump osteotomy. All patients underwent lateral and median osteotomies. Doyle or Tellez nasal splints were left in place for five to seven days and no additional nasal packing was used otherwise. Postoperatively, the patient's head was elevated and ice packs were administered for 48 h. Acetaminophen was the only analgesic used to control postoperative pain. Antibiotics were administered for seven days.

Follow-up

Each patient was digitally photographed on postoperative days 1, 3, 7 and 14. Their photos were saved in an Access database (Microsoft Corporation, USA) along with important details of the surgery and

Figure 2) Ecchymosis classification: The score awarded to each area is added to a final score that ranges from 0 to 13

the postoperative period such as intraoperative bleeding, duration of the surgery, complications, mean blood pressure, patient's postoperative care special characteristics and side effects, among others.

An external observer was instructed to grade and classify the superior and inferior eyelid edema and ecchymosis in each one of the photos according to the grading system presented in the present report (Figures 1 and 2). A detailed data sheet was completed for each patient.

Statistical analysis

Means and SDs, as well as medians and interquartile ranges were calculated for continuous variables as appropriate. Median scores were compared using Mood's median test and mean scores were compared using the T test. All statistical analysis was performed using SPSS version 20 (IBM Corporation, USA); $P < 0.05$ was considered to be statistically significant.

RESULTS

A total of 54 female patients who underwent closed rhinoplasty with median and lateral osteotomies as well as hump reduction were included in the present study. Twenty-eight patients were given steroid injection and 26 were in the placebo group. The mean ($\pm$ SD) age was 28.5 ± 9.15 years. Results regarding postoperative edema and ecchymosis on postoperative days 1, 3, 7 and 14, as well as intraoperative bleeding and operative time are presented in Table 2.

There was no statistically significant difference between the steroid and the placebo group regarding recuperation time in terms of edema and/or ecchymosis up until postoperative day 14. There was a statistically significant reduction in operation time in the intervention group compared with the placebo group. A comparative plot showing placebo versus steroid intervention with regard to ecchymosis is presented in Figure 3.

The patients included in the present study reported no major steroid-related complications. Only two patients presented with exacerbation of previous acne that subsided after the effects of the steroids dissipated.

DISCUSSION

Osteotomies are basically a form of (controlled) trauma with a considerable disruption of the abundant blood vessels in this facial region and,

TABLE 2
Results of parameters studied

	Group		P
	Steroid (n=28)	Placebo (n=26)	
Upper and lower eyelid and facial edema			
POD 1	0 (0–0)	0 (0–0)	0.504
POD 3	1 (1–2)	2 (1–3.5)	0.173
POD 7	0 (0–1)	1 (0–2)	0.636
POD 14	0 (0–0)	0 (0–0)	0.970
Upper and lower eyelid and facial ecchymosis			
POD 1	0 (0–0)	0 (0–0)	0.947
POD 3	4 (2–5)	3.5 (2–8)	0.800
POD 7	2 (1–3)	1 (0–4)	0.166
POD 14	0 (0–1)	0 (0–0.25)	0.661
Operation time, min	110.3±11.4	117±9.9	0.02
Intraoperative bleeding, mL	74.2±8.1	78.5±9.2	0.13

Data presented as median (interquartile range) or mean ± SD unless otherwise indicated. POD Postoperative day

therefore, are associated with undesirable effects (11,14). Edema and ecchymosis are main concerns for patients after rhinoplasty (4). The use of intramuscular or intravenous steroids either before or after rhinoplasty is common based on the belief that they ameliorate these unwanted effects. We believe, similar to many other practices in medicine, that this is implemented somewhat empirically in terms of dosage and frequency.

Previous randomized controlled trials have implemented prednisone (4,17), methylprednisolone (2,9-11), betamethasone (2) and dexamethasone (2-5,14,16), among others, and have suggested better results if high and repeated doses are given versus placebo, in most cases (1-5,9,10). Most reports present isolated findings of one type of steroid compared with placebo; two studies, however, have reported conflicting results. In 1991, Hoffman et al (18) reported findings using a combination of steroids, with an initial 10 mg dose of dexamethasone before surgery and complementary oral prednisolone doses that started at 50 mg and were tapered by 10 mg each day. Their results appear to be somewhat biased by the fact that their patients were allowed to use ibuprofen as needed in both arms of the study, without standardization of the dose. Nevertheless, they reported statistically significant reduction of upper and lower eyelid edema and ecchymosis on postoperative days 1 to 4 compared with placebo. Later, Gürelek et al (2) published a randomized controlled trial that included different types of anti-inflammatory drugs: three steroids – betamethasone, dexamethasone and methylprednisolone – all administered in equivalent doses and one nonsteroidal anti-inflammatory drug, tenoxicam. Ultimately, methylprednisolone was superior to other steroids and placebo but only with regard to edema.

Few contradictory reports have been published. In 1998, Berinstein et al (19) reported that patients treated with a single dose of dexamethasone presented with an increase in tissue thickness compared with placebo on measurements made through preoperative and postoperative magnetic resonance imaging scans. That study was the only one that presented an objective measurement, as opposed to all other studies found in the literature for which edema and ecchymosis are measured subjectively through scales. Additional evidence against the benefits of steroids was presented in the study by Totonchi et al (15), which suggested that steroids are not superior to arnica during the late postoperative period. A recent meta-analysis failed to show benefits of the use of steroids after postoperative day 3 (1,12). Currently, there is still no consensus on the use of steroids and it is not the standard of care for all facial plastic surgeons. Given the absence of a gold standard treatment for postrhinoplasty edema and ecchymosis, the present study was placebo controlled.

We demonstrated only a trend toward reduction in edema and ecchymosis with the use of long-acting steroids compared with placebo. This was in accordance with our perception that there was no

Figure 3) Ecchymosis score plot showing differences between the placebo and steroid groups

observed clinical difference or benefits reported by patients. Differences in intraoperative bleeding were not significant and operating time was reduced significantly in the steroid group; however, we do not have an explanation for this.

Given our results, future studies should focus on the benefits and risks of exposing healthy patients to large repeated or long-acting doses of potent steroids. Although no severe side effects were observed in our series, they should be kept in mind, specifically, hypothalamic-pituitary-adrenal axis and adrenal suppression (20). Future studies could focus on impairment of restoration and healing of tissues with prolonged and high-dose steroid use.

Limitations to the present study included the inability to measure serum steroid levels after administration, and how they may have varied according to patient age, renal function, hepatic function or other aspects of their metabolism.

CONCLUSION

The use of long-acting, single-dose dexamethasone (16±4 mg) in the perioperative period did not prove to be superior to placebo in reducing edema and ecchymosis in the postoperative period at days 1, 3, 7 and 14.

DISCLOSURES: The authors have no financial disclosures or conflicts of interest to declare. The products mentioned were used for academic purposes. The authors do not have any affiliation with the companies that produce or commercialize these products, nor is it their purpose to publicize them.

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