Analysis of the Effects of Isotretinoin on Rhinoplasty Patients

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Abstract

Background: Although the number of cosmetic surgeries performed per year continues to increase, many candidates have skin problems. Thick-skinned rhinoplasty patients pose a real challenge for surgeons. Fear of performing surgery in patients with a history of isotretinoin use is another concern.

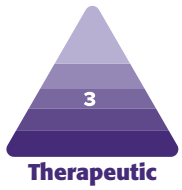
Objectives: The aim of this study was to study the effects of perioperative isotretinoin on rhinoplasty patient outcomes.

Methods: This research was conducted on 350 rhinoplasty patients, divided into control and experimental groups, between 2012 and 2015. The experimental group patients were requested to consume isotretinoin from 2 weeks before surgery to 2 months following the surgery. A comparison was made between the 2 groups 1, 3, 6, and 12 months after the surgery.

Results: Statistical tests indicated that the satisfaction of experimental group patients at months 1 and 3 following the surgery was significantly higher than that of control group patients ($P < 0.01$). Examination of the patients' noses found little evidence for soft tissue repair disturbance and cartilaginous deformities. Nine patients from the experimental group needed revision surgery during the study period, but none of the revision surgeries was for a cause clearly attributable to the intake of isotretinoin.

Conclusions: The results of this research suggest that isotretinoin causes no evident disturbance to the recovery of rhinoplastic incisions and internal nose structures. Moreover, none of the experimental group patients showed hypertrophic tissues and cartilaginous deformities, and the repair was satisfactory, similar to the control group. However, patients receiving isotretinoin were more satisfied with their operation outcomes and experienced fewer skin problems.

Level of Evidence: 3



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Rhinoplasty is one of the most common cosmetic surgeries performed to reduce and alter the shape of the nose and to correct its deformities.[1] This surgery is among top 10 cosmetic surgeries in the United States[2] and is one of the commonest cosmetic surgeries in Iran. According to the International Society of Aesthetic Plastic Surgery's (ISAPS) international survey on aesthetic procedures performed in 2013, Iran had the fourth highest number of rhinoplasties in the world with more than 37,000 performed.[3] There are

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probably many more cases, however, because the ISAPS statistics are based on a questionnaire survey completed by plastic surgeons. According to data from insurance organizations, there were more than 134,000 cases of rhinoplasty in 2010 in Iran[4] and because only a proportion of rhinoplasty procedures, including septal deviations, are covered by insurance organizations, we believe that more than 200,000 rhinoplasties are performed in Iran each year. With regards to the 2017 ISAPS statistics for other countries,[5] we think that in the absence of confirmed official data, Iran could potentially have the highest number of rhinoplasties worldwide.

Patients who seek rhinoplasty are usually young and some of them have oily skin, especially facial skin covered in acne. Isotretinoin is a drug prescribed for patients with oily skin and acne to reduce acne.[6] Isotretinoin was first approved for the treatment of severe nodular cystic acne by the US Food and Drug Administration in 1982 and has been successfully used to treat acne for many years. It is also indicated for the treatment of most forms of acne, rhinophyma, the end stage of acne rosacea, and sebaceous hyperplasia. Isotretinoin causes a significant reduction in sebum production and comedogenesis, and decreases hyperkeratinization and production of *Propionibacterium acnes*.[7] On the other hand, this drug has side effects that lead to some practitioners not recommending prescription of it for candidates for cosmetic surgeries such as rhinoplasty. Isotretinoin's side effects include teratogenicity and mucocutaneous, ophthalmologic, gastrointestinal, and neuromuscular problems. Because isotretinoin is a vitamin A analogue, many of its side effects are similar to hypervitaminosis A symptoms, including xerosis, cheilitis, granulation tissue, dry nose, epistaxis, alopecia, dry eyes, papilledema, abdominal pain, headache, fatigue, elevated lipids, and elevated liver function tests. In rhinoplasty patients, formation of keloid tissues and disrupted repair of the nose tip cartilage are worrisome cited side effects.[8]

The notion that systemic isotretinoin taken within 6 to 12 months of cutaneous surgery contributes to abnormal scarring or delayed wound healing is widely taught and practiced.[9] This belief stems from 3 case series published in the mid-1980s describing a total of 11 patients with delayed healing and keloid development following mechanical dermabrasion (10 patients) and argon laser treatment (1 patient).[10-12] The first author of this article (S.Y.) has inevitably operated on patients with a history of isotretinoin intake during years of treating patients with thick skin. Lack of visible repair problems in these patients led us to conduct a prospective study to investigate more precisely the possible side effects of isotretinoin on rhinoplasty candidates.

Reduced nose size, skin thickness and oiliness, and recovery from acne during the postoperative period in rhinoplasty cases with a history of isotretinoin use, motivated us to examine the advantages as well as possible side effects of this drug on rhinoplasty patients.

METHODS

This research was carried out as a prospective study on 350 rhinoplasty candidates, assigned to either a control or an experimental group, from July 2012 to September 2015 in Tehran, Iran. All aspects of this research were conducted in accordance with the Declaration of Helsinki and patients' written informed consent was obtained at the beginning of study.

All patients with thick and oily skin, large and fleshy nose tips, with or without acne were included in this research. The skin of patients was examined simultaneously by the first author (S.Y.) and by a dermatologist (M.I.). Skin oiliness and severity of acne were measured and compared before and after the surgery. The exclusion criteria for this research were diagnosed sensitivity to isotretinoin or other well-known contraindications of isotretinoin use (pregnancy, metabolic disturbances, drug addiction, unreliable patients, etc). To reduce the number of possible confounding variables, the research participants were randomly assigned to experimental and control groups with the QuickCalcs online randomization calculator.[13] All of the female experimental group patients were given a pregnancy test, and all of the experimental group patients had their lipid profile, liver function, and creatine phosphokinase level measured before starting the drug and at the end of study. A comprehensive explanation about oral isotretinoin usage and its possible side effects was given and prevention recommendations discussed with all of the experimental group patients. Patients of the experimental group were asked to take one 20-mg isotretinoin capsule daily after a meal (ie, approximately 0.3 mg/kg/day of isotretinoin) from 2 weeks before the surgery to 2 months following the surgery. In Iran, patients can obtain isotretinoin from certain pharmacies with a prescription from a relevant specialist. At the beginning of the research, equal numbers of patients (n = 175) were put in the control and experimental groups. However, some of the patients did not collaborate in the follow-up sessions, leaving 149 patients in the experimental group and 154 in the control group. Scheduled follow-up visits were performed by both specialists at months 1, 3, 6, and 12 following the surgery. Postoperative photographs also were taken at months 6 and 12 after surgery and compared with preoperative photographs.

During the surgery, only autogenous cartilage grafts were used for all patients. Cartilage strut was placed in 100% of patients and alar reduction performed on 98% of patients. All of the surgical operations were carried out by an endonasal approach under general anesthesia by a

Table 1. Comparison of Differences Between Variables in the Control and Experimental Groups Using the Chi-Square and Independent *t* Test Methods

	Chi-square test					Independent *t* test	Spearman's test
	Preoperative	Postoperative					
		1st month	3rd month	6th month	12th month	Comparison of total average scores	Correlation between satisfaction and variables
Facial skin oil	$P > 0.05$	$P < 0.05$*	$P < 0.05$*	$P > 0.05$	$P > 0.05$	$P > 0.05$	$R = 0.749$
Facial acne	$P > 0.05$	$P < 0.05$†	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P < 0.05$*	$R = 0.826$
Satisfaction with operation	—	$P < 0.0$*	$P < 0.01$*	$P > 0.05$	$P > 0.05$	$P < 0.05$*	—
Cartilage displacement	—	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$	—	—
Scar healing	—	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$	—	—
Keloid tissue	—	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$	—	—

*Significant difference in favor of isotretinoin use. †Significant difference in favor of control group.

single surgeon (S.Y.). After the surgery, the following variables were assessed by the surgeon and dermatologist simultaneously: patients' satisfaction with the appearance of their nose (on a Likert scale of 1-10), facial skin oiliness (on an arbitrary scale of 1-5), severity of facial acne (on an arbitrary scale of 1-5), qualitative assessment of healing of surgical incisions, possible deformities of nasal cartilages, and possible formation of keloid tissues. Analysis of data was carried out with SPSS Statistics for Windows, version 21.0 (IBM Corp, Armonk, NY) based on proper statistical tests.

RESULTS

Of the initial 350 cases, 149 patients in the experimental group and 154 in the control group (totally 303 patients) completed the study and included in the analysis. The average age of the participants was 24.3 years (range, 18.3-36.9 years) and 25.2 years (range, 18.7-39.2 years) in the experimental and control groups, respectively. A total of 107 patients (72%) in the experimental group and 108 (70%) in the control group were female. Scheduled follow-up visits were performed by both specialists at 1, 3, 6, and 12 months following surgery. During the study period no patients experienced major complications, but cheilitis, xerosis, and headache were reported in 20, 8, and 2 cases respectively. A chi-square test revealed that the satisfaction of patients at 1 and 3 months following surgery was significantly higher in the experimental group than in the control group ($P < 0.01$). This difference remained slightly higher in favor of the experimental group 6 and 12 months following the surgery. The level of satisfaction of patients of the 2 groups at the 12-month follow-up was significantly higher than the satisfaction of patients 1 month after the surgery. The facial skin oiliness of patients in the experimental group in months 1 and 3 following surgery was lower than in the control group, but levels of skin oil at the 6- and 12-month follow-ups were equal. Moreover, the facial skin oil of patients in the experimental group at months 1 and 3 after the surgery was significantly lower than the level of oil before the surgery ($P < 0.05$). Severity of acne was considerably higher in the first month after the surgery in the experimental group than in the control group ($P < 0.01$). However, at the 3- and 6-month follow-ups the severity of acne in the experimental group was lower than in the control group, but the difference was not statistically significant. In the final examination, the severities of facial acne in the 2 groups were equal and were assessed to be similar to preoperative facial acne levels. Table 1 presents the results of the comparison between variables for the control and experimental groups.

The scores of the discussed variables in all of the 4 follow-up examinations (ie, 1, 3, 6, and 12 months after surgery) were summed and the average scores of the 2 groups were compared through independent *t* test. The results of this test indicated that the experimental group patients had a higher average satisfaction than the control group patients within 1 year ($P < 0.05$), and the total average frequency of facial acne in the experimental group was lower than in the control group ($P < 0.05$). The comparison between the average total scores of other variables showed no significant difference ($P > 0.05$). In addition, a Spearman's test revealed a direct negative correlation between "satisfaction with operation" and other variables (Table 1). For instance, with a decrease in severity of facial acne, the satisfaction score of patients with surgery

increased (experimental group), whereas with an increase in the severity of acne, the satisfaction score of patients with surgery decreased (control group).

Qualitative assessment of the healing status and possible deformities of nasal cartilages indicated that in none of the cases was the repair process delayed, and it occurred properly and naturally. None of the participants showed cartilage deformities. No keloid tissue was seen in the surgical incisions (inside the nose or alar resection scar) of the participants. All of the patients in the experimental group showed a significant improvement in the appearance and texture of the skin of their nose and face. Their nasal tips appeared a lot more defined than in their presurgical images. None of the patients who experienced alar resection had visible scarring or abnormal scars, and none of these patients received any additional type of treatment to reduce scarring (Figures 1-4 and Supplemental Figures 1-5, available online at www.aestheticsurgeryjournal.com).

Of the research participants, 19 cases needed reoperation within the study period (3 years), 9 of which were from the experimental group and 10 from the control group. The causes of revision surgeries in these patients

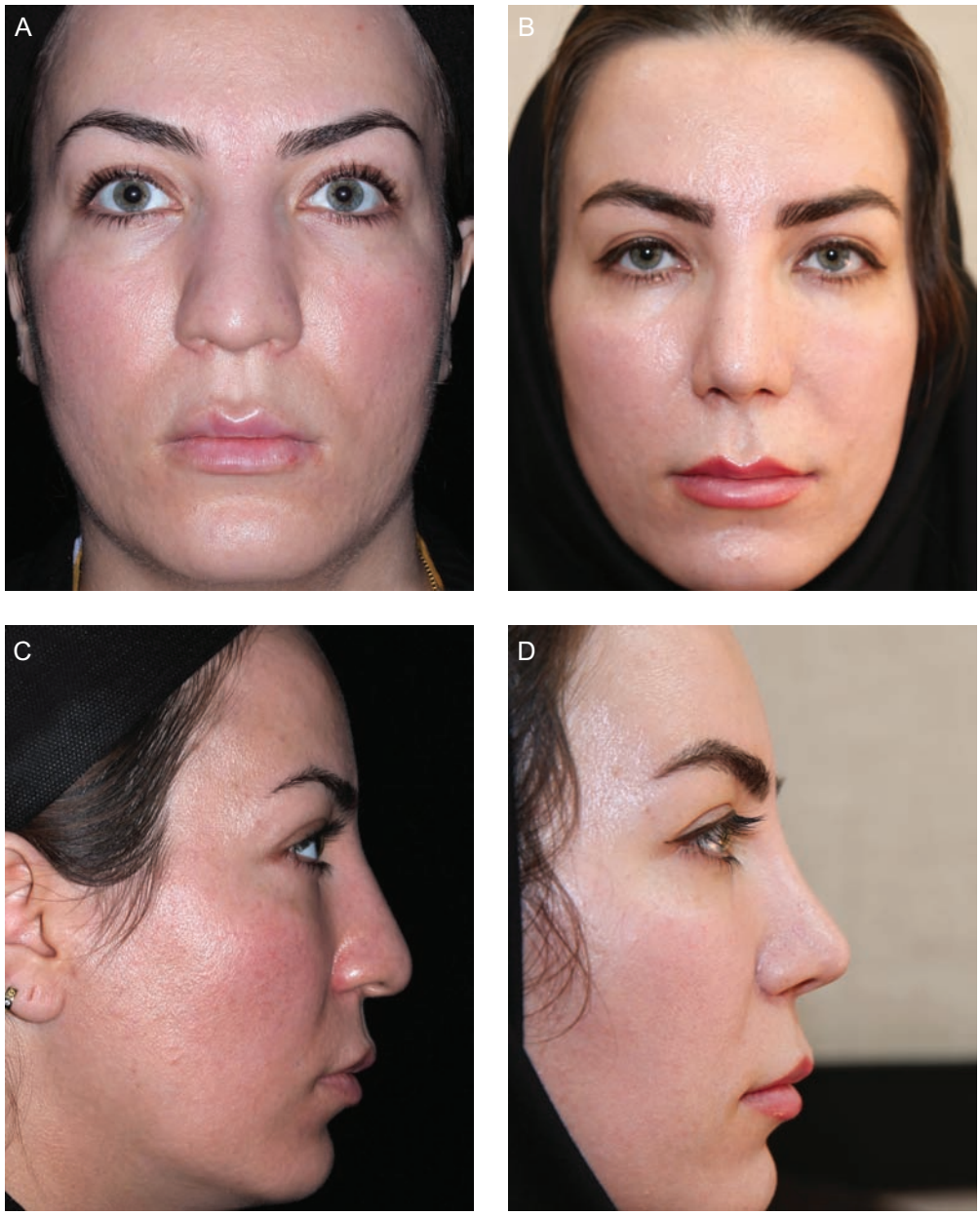

Figure 1. (A, C) Preoperative and (B, D) 2-year postoperative photographs of a 35-year-old female patient treated with isotretinoin preoperatively and postoperatively.

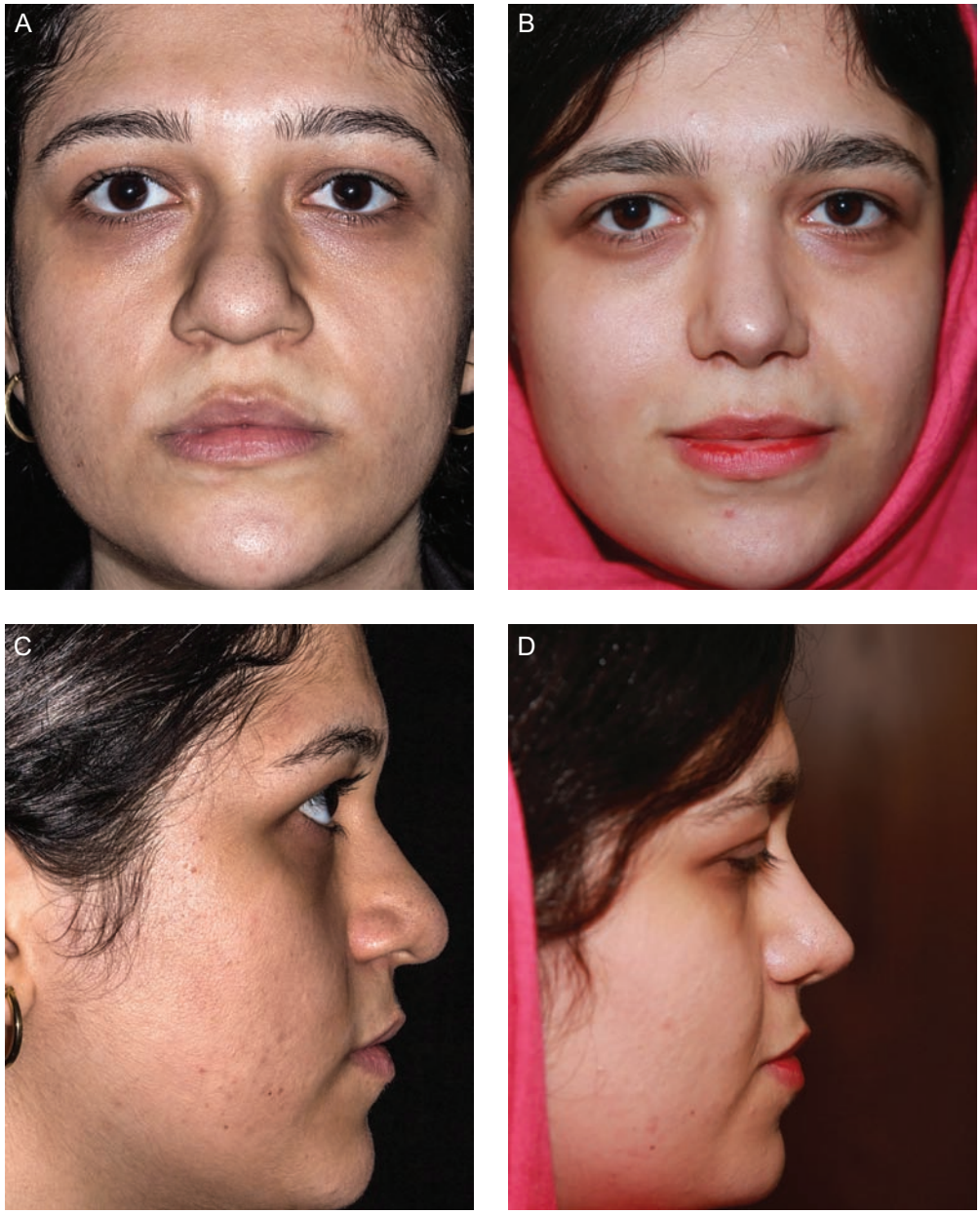

Figure 2. (A, C) Preoperative and (B, D) 2-year postoperative photographs of a 24-year-old female patient treated with isotretinoin preoperatively and postoperatively.

could not be attributed to consumption of isotretinoin. The causes of reconstructive surgeries were tip irregularities in 4 patients, a large nose tip in 4 patients, dorsal lumping in 5 patients, nasal axis deviation in 4 patients, and asymmetric nostrils in 2 patients.

DISCUSSION

Numerous studies have been carried out on treatment with isotretinoin and repair of surgical skin scars. Some authors have asserted that systematic consumption of isotretinoin leads to granular tissue formation, formation of keloid tissue, and disturbed wound recovery.[14,15] Avoidance of isotretinoin in the perioperative period of facial resurfacing was adopted as a medicolegal standard in the 1980s after the report by Rubenstein et al and others.[10-12] Since then, researchers have suggested that isotretinoin should be withheld for 6 to 24 months before surgery. Plastic surgeons also adopted these recommendations based on the recommendations of dermatologists.[16]

The study by Allen and Rhee[17] is the most-cited recent article about complications of isotretinoin therapy in rhinoplasty patients. In their retrospective review, 3 cases of tip

Figure 3. (A, C) Preoperative and (B, D) 1-year postoperative photographs of a 21-year-old female patient treated with isotretinoin preoperatively and postoperatively.

deformities were attributed to isotretionin use within 2 years of surgery. Two of these cases were tip bossae (1 was revision surgery and 1 included conchal cartilage graft) and 1 was a complication of an auricular composite graft. Unlike those authors, we believe that there is no rationale to consider a "causal effect" between isotretinoin and these patients' complications. For example, even thinning of the skin is not a good explanation for obvious domal asymmetry in their case number 3. We believe that the problems in their patients more probably relate to surgical technique.

It has been documented that when rhinoplasty is performed, acne is increased by 27% in the first month after surgery in comparison with patients who underwent only functional nasal surgery.[18] Other reasons for acne exacerbation can be irregular cleansing routines and prolonged use of nasal tapes.[7] In our study, the examinations carried out 3 and 6 months following surgery showed higher postoperative satisfaction in patients consuming isotretinoin, which can be attributed to the antiacne and skin-oil-reducing effects of this drug. Statistical tests also showed a strong correlation between these variables. However, at the end of follow-up, the point-to-point satisfaction of patients of both groups was comparable. Patients who received isotretinoin were satisfied earlier during the first postoperative months,

Figure 4. (A, C, E) Preoperative and (B, D, F) 1-year postoperative photographs of a 33-year-old female patient treated with isotretinoin preoperatively and postoperatively.

whereas patients of the control group reached that level of satisfaction at later months. Satisfaction of patients with their noses statistically and negatively correlated with variables such as facial acne and oily skin. In other words, with a decrease in the oily skin score or acne score (as a result of consumption of isotretinoin), the score of satisfaction with the operation increases.

Guyuron and Lee[19] propose that isotretinoin delays healing and that any invasive maneuvers, such as dermabrasion, laser, or surgery, should be delayed for at least 1 year; but rhinoplasty could be considered about 6 months following termination of the drug. However, Ungarelli et al[16] in their conclusive study evaluated current evidence about 11 important aspects of isotretinoin use in surgical patients. After examining 47 related studies in their work, they concluded that "the reported data lead to the notion that isotretinoin does not promote skin healing issues." They also have criticized the currently recommended time between discontinuation of isotretinoin and surgery. Considering isotretinoin pharmacokinetics, they believe that discontinuation of this drug for 30 to 35 days before surgery is a justifiable delay.

The dosing regimen of isotretinoin also has been debated. The standard dosage is determined by weight and

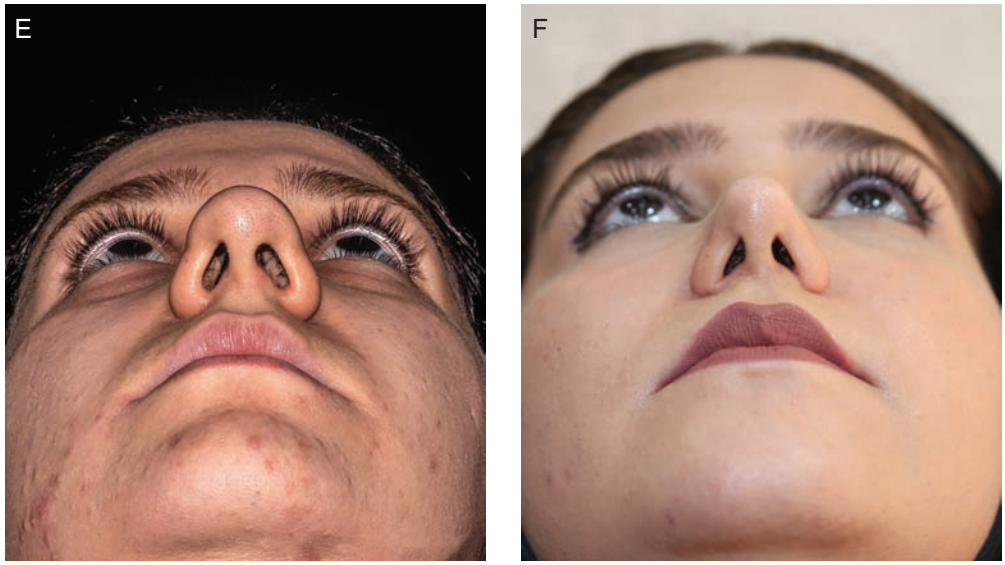

Figure 4. Continued.

usually ranges from 0.5 to 1.0 mg/kg daily to reach a total dose of 120 to 180 mg/kg. However, several studies proposed that a low-dose regimen of <0.5 mg/kg is as efficient as the standard dosing regimen and may offer the advantages of increased tolerability and patient adherence. The most common low-dose isotretinoin schemes involve dosages from 0.25 to 0.5 mg/kg daily.[20]

We used a daily dose of nearly 0.3 mg/kg which is in agreement with other proposed regimens.[21] Micro- and mini-dosing schedules also have been published with 10 to 20 mg per day once or twice weekly.[20]

Although Kosins and Obagi[21] have used isotretinoin 3 to 4 weeks after surgery and continued it for 4 to 5 months, we started it before surgery to make use of its ability to control oiliness during the early postoperative period and discontinued it after 2 months. Most studies believe that the duration of treatment should be at least 4 to 6 months,[7,21] whereas we used it for 10 weeks in total without repeating. We think that most of the benefits of isotretinoin occur in the immediate postoperative period. Meanwhile, we agree that relapse rates are not affected by using a reduced-dosing scheme but intermittent dosing is associated with higher relapse rates.[7]

As limitations of our study, it is worth mentioning that the present research was only carried out on rhinoplasty patients, who experienced limited facial skin incisions, and thus further extensive research is required to generalize these results to all skin surgeries. Moreover, quantitative studies to measure skin thickness following isotretinoin consumption after rhinoplasty would be of value.

CONCLUSIONS

Isotretinoin does not appear to induce major nose repair and recovery problems following rhinoplasty. Hence, there is no need to postpone rhinoplasty in patients with a history of consumption of isotretinoin. However, we strongly believe that it is possible to use the positive effects of this drug to reduce skin thickness, skin oil, and acne in patients with oily and thick skin with or without acne before surgery. Based on our experience and observations during years of surgery, we assert that isotretinoin has the following advantages in addition to the advantages discussed above: no early detachment of the nose plaster or splint (which is commonly seen in patients with oily skin and sometimes leads to severe inflammation of the nose tip); a stronger bond between tape and nose skin; and accelerated recovery after surgery, especially in the early weeks (which increases patient satisfaction during this period).

Supplemental Material

This article contains supplementary material located online at www.aestheticsurgeryjournal.com.

Disclosures

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