Guidelines

Standard Guidelines of Care: Performing Procedures in Patients on or Recently Administered with Isotretinoin

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Abstract

Background: Currently, the standard protocol regarding the performance of procedures on patients receiving or having recently received isotretinoin (13-cis-retinoic acid) states that the procedures should not be performed. The recommendations in standard books and drug insert require discontinuation of isotretinoin for 6 months before performing cosmetic procedures, including waxing, dermabrasion, chemical peels, laser procedures, or incisional and excisional cold-steel surgery. These recommendations have been followed for over two decades despite little evidence for the stated increased risk of scarring. Objective: The Association of Cutaneous Surgeons (I) constituted a task force to review the evidence and to recommend consensus guidelines regarding the safety of skin procedures, including resurfacing, energy-device treatments, and dermatosurgical procedures in patients with concurrent or recent isotretinoin administration. Materials and Methods: Data were extracted from the literature through a PubMed search using the keywords “isotretinoin,” “safety,” “scarring,” “keloids,” “hypertrophic scarring,” and “pigmentation.” The evidence was then labeled and circulated to all members of task force for review. Results: The task force is of the opinion that there is insufficient evidence to support the current protocol of avoiding and delaying treatments in the patient group under consideration and recommends that the current practice should be discontinued. The task force concludes that performing procedures such as laser hair removal, fractional lasers for aging and acne scarring, lasers for pigmented skin lesions, fractional radio-frequency microneedling, superficial and medium-depth peels, microdermabrasion, dermaroller, biopsies, radio-frequency ablation, and superficial excisions is safe in patients with concurrent or recent isotretinoin administration.

Keywords: Dermatosurgical procedures, guidelines, isotretinoin, safety

BACKGROUND

Isotretinoin, a retinol derivative of vitamin A widely used in the treatment of acne vulgaris, has many pharmacological actions that affect epidermis, sebaceous gland, and collagen formation. The propensity of isotretinoin to affect these functions has led to questions about the possibility of poor wound healing, keloid development, and hypertrophic scarring, particularly in patients who undergo dermatosurgical procedures while on this drug. A detailed discussion of the mechanisms of action of the drug with respect to wound healing and scar formation has been reported in several standard publications, to which the reader is referred to.[1-5]

It has been the standard recommendation for over two decades that it is not safe to perform procedures in patients currently receiving or having recently completed systemic therapy with isotretinoin as the drug affects healing of wounds and hence may lead to hypertrophic scarring and keloid formation. Although this has generally been adhered to by practitioners, the recommendation has been questioned by a number of studies that have documented...
safety of cutaneous procedures in such patients. The Indian skin is brown and reacts differently to procedures with pigmentation. Hence, it was felt that there is a need for guidelines oriented to the Indian situation. The Association of Cutaneous Surgeons (I), as part of a presidential project by the then President Dr. Venkataram Mysore, conducted a multicentric study to examine the issue in the Indian setting, the findings of which were published recently. A task force was then constituted to formulate and recommend new guidelines appropriate to brown skin.

**Materials and Methods**

The task force performed a PubMed search using the keywords “isotretinoin,” “isotretinoin side effects,” “isotretinoin,” AND “laser”; “isotretinoin” AND “surgery”; “isotretinoin” AND “keloid”; “isotretinoin” AND “wound healing”; “Isotretinoin” AND “hypertrophic scarring, isotretinoin, and pigmentation.” A total of 403, 62, and 27 articles were found with respect to “isotretinoin” AND “surgery”; “Isotretinoin” AND “wound healing”; and “Isotretinoin” AND “laser,” respectively. Of these, 27 articles were found to be of relevance as they specifically referred to the issue of scar formation and keloids. The task force took into account recent consensus guidelines published by other associations such as the American Society for Dermatologic Surgery and a task force by JAMA (Journal of American Medical Association). The publications were studied in depth with respect to the evidence levels (as per Harbour and Miller’s revised grading system [Table 1]).

**Existing Guidelines**

All standard textbooks[1-3] state that performing dermatological procedures is not safe in patients currently or recently administered with isotretinoin and that a safe window period of 6 months after stopping the drug is advisable before performing procedures.

The patient information leaflet of the drug advises patients to “avoid chemical dermabrasion and laser treatment of the skin and wax depilation during and for at least 6 months after treatment as they could cause scarring or irritation of the skin.”[4]

The US Food and Drug Administration (FDA) also advises patients as follows: “Do not have cosmetic procedures to smooth your skin, including waxing, dermabrasion, or laser procedures, while you are using Accutane and for at least 6 months after you stop. Accutane can increase your chance of scarring from these procedures. Check with your doctor for advice about when you can have cosmetic procedures.”[5]

**Historical basis for the existing guidelines**

Some studies, mostly case reports from the 1980s to the 1990s, document delayed healing, hypertrophic scarring, and keloid formation after procedures in patients on oral isotretinoin.[6-10] The data of these studies, along with their evidence level, are shown in Table 2. During the same period, several other in vitro studies have shown that wound-healing processes can be affected by the administration of retinoids, topically and systemically.[11-15]

Detailed examination of these studies shows that these are all limited studies in a small number of patients, or isolated case reports of an inadequate number of procedures that were mostly aggressive procedures or conducted with early generation laser devices. The evidence would at best qualify for level 3. Furthermore, these studies were conducted with respect to only certain procedures such as argon laser

### Table 1: Harbour and Miller’s revised grading system for recommendations in evidence-based guideline

| Levels of evidence in literature: 1++ to 4 |
|------------------------------------------|
| A. At least one meta-analysis, systematic review, or RCT rated as 1++ and directly applicable to the target population or a systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+ directly applicable to the target population and showing overall consistency of results |
| B. A body of evidence including studies rated as 2++ directly applicable to the target population and showing overall consistency of results or extrapolated evidence from studies rated as 1++ or 1+ |
| C. A body of evidence including studies rated as 2+ directly applicable to the target population and showing overall consistency of results or extrapolated evidence from studies rated as 2++ |
| D. Evidence level 3 or 4 or extrapolated evidence from studies rated as 2+ |

From Harbour R, Miller J. A new system for grading recommendations in evidence based guidelines. BMJ 2001;323:334–6.
Table 2: Old studies on oral isotretinoin intake and scarring postinterventions: summary of data with evidence levels

| Year of publication | Journal | Purpose of publication | No. of patients treated | Oral isotretinoin | History of hypertrophic scar present | Duration of follow-up | Site of dermabrasion/laser | Complications | Limitations of study | Evidence level |
|---------------------|---------|-------------------------|-------------------------|-------------------|-------------------------------------|-----------------------|--------------------------|---------------|----------------------|----------------|
| 1985[6]             | J Dermatol Surg Oncol 11:396–8 | Acne, retinoids, and dermabrasion. | 9 | Concomitant isotretinoin | | 9 days | Rhinophyma dermabrasion | No complications. | Case series | 3 |
| 1986[7]             | J Am Acad Dermatol 15:280–5 | Dermabrasion on face | 3 | | | 1–3 months | Face | 1–3 months noted keloids on face. Resolved in 2 patients with interventions. | Case report | 3 |
| 1988[8]             | Br J Dermatol 118: 703–6 | Delayed wound healing and keloid formation following argon laser therapy or dermabrasion | Patient 1 | On isotretinoin | Yes | 8 months | Face, argon laser for rosacea | Delayed scarring. | Case report | 3 |
| 1994[9]             | J Am Acad Dermatol 30:852–3 | Dermabrasion on face and later intake of oral isotretinoin. | 1 | Intake of oral isotretinoin after dermabrasion | No | | Face | Keloid | Single case | 3 |
| 1997[10]            | Arch Dermatol 133:111–2 | Pulse dye laser induced keloid in a case on isotretinoin. | 1 | | | | Face | keloid | | 3 |
Lasers for resurfacing

Fractional lasers (ablative lasers \([\text{CO}_2\text{]}\) and erbium-doped yttrium aluminum garnet (Er:YAG) laser) and nonablative lasers erbium glass) are used for postacne scarring. Lasers for acne scarring are a more aggressive treatment than laser hair removal as the target tissue is collagen and thus it affects collagen synthesis. However, several studies have been conducted that do not confirm any risk for development of keloids or hypertrophic scars.\(^{[24-28]}\)

*Level of evidence in literature: 2++*

*Recommendation:* The task force recommends that fractional ablative and nonablative lasers can be used safely among patients on isotretinoin.

*Recommendation level:* Grade B

Laser procedures for other indications

A single case where a patient who had acne vulgaris with nevus of hori underwent four sessions with q-switched Nd:YAG laser and showed no evidence of hypertrophic scar or keloid formation.\(^{[27]}\)

*Level of evidence in literature: 3*

*Recommendation:* Because q-switched lasers cause limited damage to the epidermis as well as dermal collagen and because there are no documented studies of any adverse events with this laser, the task force recommends that the procedure can be safely performed in patients.

*Recommendation level:* Grade D

Dermabrasion and full-face ablative \(\text{CO}_2\) laser resurfacing

Dermabrasion and ablative \(\text{CO}_2\) laser resurfacing are perhaps the most invasive cutaneous aesthetic procedures, though seldom used after the advent of fractional lasers, particularly in the Indian setting. Early reports indicated the development of hypertrophic scarring after dermabrasion, and in fact was responsible for the recommendation currently being followed.\(^{[7-9]}\) However, one recent study suggested that the procedure is safe without any tendency for hypertrophic scarring.\(^{[29]}\)

*Level of evidence in literature: 2+*

*Recommendation:* The task force feels that dermabrasion and full-face \(\text{CO}_2\) laser resurfacing as a treatment modality is not widely performed in current practice as safer options are available and any recommendation is not relevant in this procedure. If any physician still wishes to resort to this procedure, it would be safer to wait for the window period of 6 months after stopping the drug, and the procedure performed after receiving the appropriate informed consent and following protocols.

*Recommendation level:* Grade C
| Year of publication | Journal                          | Purpose of publication                                                                 | No of patients treated | Oral isotretinoin | History of hypertrophic scar present | Duration of follow-up | Site of procedure | Complications | Limitations of study             | Evidence level |
|---------------------|----------------------------------|-----------------------------------------------------------------------------------------|------------------------|------------------|-------------------------------------|-----------------------|-------------------|---------------|----------------------------------|----------------|
| 2000[16]            | Dermatol Surg 26:649–52          | Efficacy of isotretinoin in addition to procedures while treating cutaneous aging         | 60                     | 10–20 mg 3 times a week for 3 months | 6 months           | Face                           | None          | Had a control group                | 2++            |
| 2004[17]            | Dermatol Surg 30:1205–7          | Diode hair reduction in patients on oral isotretinoin                                    | 7                      | Concomitant 63 mg/day isotretinoin mean of 4 months duration | 1 month            | Axilla and bikini hair reduction | One patient had blister, by week one, which resolved | Case series | 2+                            |
| 2005[18]            | Dermatol Surg 31:380–381         | Diode hair reduction and oral isotretinoin                                             | 6                      | Concomitant      | 4 years                           | Facial hair reduction | Erythema immediate, crusting that resolved in few days | Case series | 2+                            |
| 2006[19]            | Dermatol Surg 32:875–7           | Light-assisted hair removal in patients undergoing isotretinoin therapy                  | ?                      | Concomitant      | none                              | Face                           | Nil               | Intervventional               | 2+             |
| 2009[20]            | J Cosmet Laser Ther 11: 56–60    | Long-pulsed Nd:YAG laser reduction in patients taking oral isotretinoin, concomitantly  | 11                     | Concomitant, but stopped during the laser therapy day | 12 weeks post laser | Face and extracranial site hair reduction | No adverse events | Retrospective case series | 2+             |
| 2010[21]            | Dermatol Surg 36:483–9           | Outcome of diamond fraise dermabrasion in patients taking oral isotretinoin              | 7                      | On the drug during intervention. Yes in one patient | 6 months postsurgery | Face                           | Nil in all and even in the case with history of hypertrophic scarring | Interventional type. No control group | 2++            |
| 2012[22]            | Dermatol Surg 38:1521–6          | Outcome after chemabrasion, in patients who had stopped isotretinoin.                   | 10                     | Stopped isotretinoin 3 months prior | 6 months post-surgery | Face                           | No hypertrophic scarring | Interventional prospective study | 2++            |
| 2013[23]            | J Cutan Aesthet Surg 6:204–8     | Salicylic acid peel with and without isotretinoin in acne patients                       | 60                     | 20 mg daily      | 16 weeks                          | Face                           | None               | Comparative study               | 2++            |
| 2014[24]            | J Dermatolog Treat 25:142–6      | 1550 nm laser fractional laser therapy                                                | 35                     | Prior intake of 10 mg/day of oral isotretinoin | No                   | Face                           | No keloid          | No control group               | 2++            |
| 2014[25]            | Int J Dermatol 53:1281–5         | Concomitant oral isotretinoin intake and performance of a) Microneedling in 12 cases b) Fractional CO2 in 25 cases c) Microneedling radio frequency in 13 cases d) Hair reduction-diode/Nd: YAG/IPL in 5 cases | 55 cases with 55 control group | 0.5 mg/kg of oral isotretinoin | No                   | Face                           | No keloid          | Good study with control group   | 2++            |

Contd...
| Year of publication | Journal | Purpose of publication | No of patients treated | Oral isotretinoin | History of hypertrophic scar present | Duration of follow-up | Site of procedure | Complications | Limitations of study | Evidence level |
|---------------------|---------|------------------------|------------------------|-------------------|-------------------------------------|----------------------|-----------------|--------------|------------------|----------------|
| 2014[26]           | Dermatol Surg 40:1361–6 | Fractional CO₂ laser facial resurfacing in patients on concomitant or past intake of oral isotretinoin. | 20 | 10–60 mg/day | No | Face | No keloid | Retrospective | 2++ |
| 2016[27]           | J Cutan Aesthet Surg 9:106–14 | Surgical outcome in patients on concomitant or past intake of oral isotretinoin. a) Fractional Er:YAG-102 sessions b) Fractional CO₂-19 sessions c) Full face ablative CO₂-19 sessions d) Laser/IPL hair reduction-38 sessions e) Peels-246 sessions f) Cold steel-microneedling, biopsy-27 sessions g) Electrosurgery—1 case. | 183 | 122 concomitant, 61 past intake of oral isotretinoin. | In one case | Face | Keloids-2, pigmentation-15 Erythema-10 | No control group | 2++ |
| 2016[27]           | Int J Dermatol 55:1255-8 | Prevalence of hypertrophic scars and keloids in acne patients treated with oral isotretinoin. | ? | Concomitant or past usage | Face | No complications | Observational retrospective | ?? |
| 2016[29]           | Dermatol Surg 41:758-9 | Laser skin resurfacing during isotretinoin therapy | 1 | One site treated each with a nonablative fractional laser, ablative fractional laser, and full ablative laser | 40 mg twice daily | Back | None- single spot | 3 |
| 2017[30]           | Dermatol Surg 43:357–63 | Complications arising in patients treated with laser while receiving isotretinoin or within 6 months of completing a course of therapy | 220 physicians | All lasers | ? | ? | Seventy-six percent of respondents had never seen any cases of complications | Survey of 220 nationally recognized experts in cutaneous laser surgery |
Chemical peeling
Chemical peels are performed for a number of indications including patients of acne and scarring. In today’s practice, superficial peels and occasionally, medium-depth peels are used. Studies have recognized the safety of salicylic acid, glycolic acid, combination peels, and trichloroacetic acid among patients on isotretinoin. However, a case report of persistent hyperpigmentation after glycolic acid peel in one patient has been published. There have been very few reports of deep peels in patients on isotretinoin, perhaps because of lack of use of deep peels in current practice.

Level of evidence in literature: 2+

Recommendation: The task force considers the superficial and medium-depth peels to be safe in patients on isotretinoin

Recommendation level: Grade C

Microdermabrasion and dermaroller
Microdermabrasion and dermaroller are increasingly used in dermatology practice for a number of reasons. These are generally minimally invasive and safe procedures. There are two studies that document the safety of procedures in patients administered with isotretinoin.

Level of evidence in literature: 2+

Recommendation: The task force recommends that microneedling and microdermabrasion treatment can safely be performed in patients administered with isotretinoin.

Recommendation level: Grade C

Radio-frequency procedures
Radio-frequency devices are used in dermatology practice either to cut/coagulate—exophytic lesions or for collagen stimulation in scars and rejuvenation. The limited data show both ablative radio-frequency and fractional microneedling radio-frequency to be safe. One single compound nevus excision on face lead to keloid.

Level of evidence in literature: 2+

Recommendation: The task force feels that superficial lesions can safely be removed by radio-frequency devices in patients administered with isotretinoin. However, for deep lesions, caution should be exercised during the window period of 6 months and such decisions should be based on the medical needs of the patient with the given condition.

Recommendation level: Grade B

Skin biopsies
Skin biopsies that involve collagen damage did not produce keloid in eight patients.

Level of evidence in literature: 2+

Recommendation: A biopsy is crucial for diagnosis and needs to be performed for medical reasons. Therefore, there cannot be a recommendation restricting this essential diagnostic procedure.

Recommendation level: Grade B

Discussion
The aforementioned review shows rather overwhelmingly that the risks of hypertrophic scarring, keloid formation, delayed wound healing, and pigmentation are not significant in most dermatological procedures. As such, the recommendation to avoid procedures in these patients was, in our opinion, based on flawed reasoning. As Goodman stated in a commentary “Many different ‘standards’ of practice dictated how long after Isotretinoin was completed it was considered safe to consider chemical peels, dermabrasion, or laser resurfacing. No science followed but many firmly held opinions ranging from 6 to 24 months were considered to be the prudent time after Isotretinoin before procedures were safe.”

The task force is of the firm opinion that such a recommendation based on poor quality evidence would never have been accepted in the current day with emphasis on evidence-based practice if it had been made. Therefore, the recommendation has only served to deny patients safe treatments and put unnecessary fear in the minds of doctors. This was confirmed by a recent survey of nationally recognized experts of laser surgery regarding the treatment of patients administered isotretinoin therapy currently or within 6 months. In this report, most of the respondents (70%) affirmed that medicolegal concerns guided their decision-making regarding this patient population, in contrast to concerns about atypical or poor wound healing (69%), scarring (66%), and hypertrophic or keloidal scarring (49%). This was despite the fact that 76% respondents had never seen any complications in their own clinical practice. It was rightly summarized by Goldman that “What becomes clear is that the overwhelming majority of physicians are curtailing laser treatments because of the fear of litigation.”

The task force, therefore, opines that the current recommendation needs to be withdrawn and summarizes its recommendations as follows:

1. There is no need to delay procedures such as laser hair removal, fractional lasers, radio frequency, microneedling, microdermabrasion for which there have never been any reports of adverse effects. These procedures can be performed safely: “Level B.”

2. Aggressive procedures such as dermabrasion, full-face ablative laser resurfacing, and deep peels, where there are small reports of adverse effects, are rarely performed in current practice, particularly in brown skin. However, if a physician still wishes to perform these procedures, caution needs to be exercised and such procedures may be performed after a window period of 6 months of stopping the drug. Appropriate
informed consent needs to be taken in such cases and the physician should follow all the protocols applicable to each procedure: “Level C.”

3. During its survey, the task force found that most of the studies quoted above used a dosage ranging between 10 and 80 mg. Although there is no evidence to judge whether higher doses carry greater risk, it may be prudent at the current time to restrict the dosage to less than 0.5 mg/kg body weight in patients: “Level C.”

The summary of recommendations for each procedure is shown in Table 4.

The task force is aware that the recommendations made here are based on level B or C evidence. It is the task force’s hope that the formulation of these recommendations will remove the apprehension from the minds of physicians and lead to more procedures being performed in patients administered with isotretinoin. This will lead to the further accumulation of evidence, and the formulation of guidelines will be based on stronger evidence in the future. It is also heartening to note that two recent guidelines[34,35] have been published on this subject and the task force concurs with those recommendations. A recent textbook edited by the first author of this article also dealt with the subject and suggested that the procedures can be safely performed in these patients.[36] In addition to this, some recent textbooks discuss at length the adverse events of isotretinoin such as inflammatory bowel disease and depression but have stopped mentioning keloid and hypertrophic scarring.[37,38]

Finally, these recommendations have been made with particular reference to Indian or brown skin. It is noteworthy that two of the largest studies[25,27] that support the recommendation have been on Indian skin.

Table 4: Summary of recommendations and grade recommendation in patients on isotretinoin

| Procedure                                | Recommendation | Grade |
|------------------------------------------|----------------|-------|
| Laser hair removal                       | Safe           | B     |
| Fractional lasers—ablative and nonablative | Safe          | B     |
| Ablative lasers—full-face resurfacing    | Caution is advised; test patch may be advised and observed for 6 months or procedure may be delayed for 6 months of isotretinoin use | C     |
| Q-switched lasers and vascular lasers    | Safe           | D     |
| Fractional microneedle radio frequency   | Safe           | C     |
| Superficial and medium-depth peels       | Safe           | B     |
| Deep peels                               | Caution is advised; test patch may be advised, and observed for 6 months or procedure may be delayed for 6 months of isotretinoin use | C     |
| Microdermabrasion, dermaroller           | Safe           | B     |
| Biopsies, superficial excisions          | Safe           | B     |
| Deep excisions                           | These conditions are medical conditions and surgery may be necessary for the health of the patients. | No recommendation required—necessity and risk for health of the patients will dictate the judgment |

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