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DROPPING THE DELAY: SAFETY OF PROCEDURAL INTERVENTIONS DURING AND AFTER ISOTRETINOIN USE

Introduction

Systemic isotretinoin is a commonly employed treatment for acne. Currently, the Health Canada approved product monograph contains a warning that aggressive chemical dermabrasion and cutaneous laser treatment be avoided in patients for a period of 5-6 months after the end of treatment because of the risk of hypertrophic scarring in atypical areas, and more rarely hyper- or hypo-pigmentation in treated areas. This recommendation, derived largely from case reports or studies conducted in the 1980s, is based on the belief that systemic isotretinoin therapy contributes to abnormal wound healing and increased risks for scarring. However, there is a growing body of evidence that sheds new light on these claims, and several groups have recently released consensus recommendations addressing these concerns. This paper aims to summarize our current understanding and the most recent evidence-based clinical recommendations regarding the safety of procedural interventions in the setting of systemic isotretinoin therapy.

Chemical Peels

Chemical peels of varying depths can be used to treat active acne lesions, dyspigmentation, and acne scarring. Several trials have reported favourable outcomes with superficial and medium depth chemical peels for patients treated with isotretinoin. In one such randomized controlled trial, 20 patients on low-dose isotretinoin were treated concurrently with a total of 45 resorcinol peels. The trial reported statistically significant improvements in hyperpigmentation and other markers of cutaneous aging.[1] Similarly, a cohort study of 10 patients with depressed acne scars, all of whom had completed isotretinoin therapy 1-3 months prior, were treated with a medium depth peel (Jessner's solution + 35% trichloroacetic acid) in addition to manual dermabrasion with sandpaper. Favourable cosmetic outcomes were reported with no adverse healing events noted.[2] A similar study looking at 30 isotretinoin patients treated with serial 20% salicylic acid peels over a course of 16 weeks reported improved acne clearance and no negative outcomes as compared to those on same-dose isotretinoin alone.[3] More recently, a comparative retrospective analysis of 47 patients on isotretinoin and treated with 3 types of superficial chemical peels (22 with salicylic acid (20%)-mandelic acid (20%), 18 patients with glycolic acid (20%-25%), and 7 patients with a

modified Jessner's peel) were compared to 13 patients not receiving oral isotretinoin but treated with these same chemical peels. There was no statistically significant difference between the groups with respect to complications (1 patient per group experienced persistent hyperpigmentation), but the group on isotretinoin experienced better overall outcomes.[4] In contrast, few reports of negative outcomes exist. One case report of severe hyperpigmentation and scarring has been reported following a 70% glycolic acid peel in a patient 3 weeks post-discontinuation of an unmonitored, self-administered course of isotretinoin.[5] Based on this data, current consensus recommendations suggest that the use of superficial chemical peels in the settling of low-dose isotretinoin is safe with no increased risk for scarring or poor wound healing.[6-8] There are no reports of deep chemical peels performed in patients with recent isotretinoin exposure, likely reflecting caution of deep peels in this patient population, and as well, the general reduction in use of this treatment modality in light of newer and safer alternatives (e.g., laser).

Dermabrasion

There are several studies documenting good outcomes with manual dermabrasion in patients treated with isotretinoin. Picosse et al documented the outcomes of 10 patients that underwent a medium depth chemical peel followed by manual dermabrasion to 1 cm^2 areas of focally depressed scarring. All patients displayed complete re-epithelialization and improvement of scarring, with only one patient displaying post-inflammatory hyperpigmentation. There were no reports of hypertrophic scars or keloids.[2] Similarly, a recent prospective study of 7 patients actively treated with isotretinoin for 1-6 months underwent manual dermabrasion to focal areas of scarring. At 180 days post-procedure, all patients displayed normal re-epithelialization with no procedure-associated scarring noted.[9] Importantly, both studies included at least one patient with a history of previous hypertrophic acne scars. Similarly, a prospective study looking at serial microdermabrasion treatments on 18 patients concomitantly on, or recently treated with, isotretinoin was performed without complication.[10]

In contrast to the above, there are several case reports and case series that caution against the use of mechanical dermabrasion in the setting of recent isotretinoin use.[11-14] In these publications, several patients were reported to have delayed wound healing and keloid development following mechanical dermabrasion, either in the context of concurrent, recent or even subsequent treatment with isotretinoin therapy. As such, current consensus recommendations suggest that microdermabrasion and manual dermabrasion is safe for those on isotretinoin or within 6 months of discontinuing this therapy. Mechanical dermabrasion should be avoided in this patient population and until at least 6 months post-treatment discontinuation.[6-8]

Fractional Ablative and Nonablative Laser

Several studies have reported on the safety and favourable outcomes for patients receiving either fractional ablative or nonablative laser in conjunction with isotretinoin. In one retrospective study, 50 patients treated with fractional CO2 laser for acne scarring were compared: 25 patients on low-dose isotretinoin and 25 patients not on systemic treatment. Follow-up at 24 weeks showed similar outcomes in both groups and no cases of abnormal wound healing or keloid formation in either group.[15] Similar findings were reported in another retrospective study looking at 20 patients (Fitzpatrick Skin Type III-IV) when followed for at least 6 months post-laser treatment.[16] A more recent prospective cohort study reported the outcomes of multiple treatment modalities including fractional erbium:yttrium-aluminum-garnet (Erb:YAG), fractional CO2, and ablative CO2 in patients concomitantly taking or having recently completed isotretinoin therapy. Of 141 fractional ablative procedures performed, there were 15 cases of post-inflammatory hyperpigmentation and one case of prolonged erythema, all of which resolved.[10] A study comparing the use of a nonablative fractional 1550-nm erbium:fiber laser in 30 patients actively taking low-dose isotretinoin to 30 patients who had completed a treatment course more than 6-months prior, showed similar outcomes.[17] More recently, a study from South Korea looked at the effects of a nonablative fractional 1550-nm erbium-doped fiber laser for acne scarring in 35 patients on low-dose isotretinoin as compared to 18 patients not on oral treatment. The study found better cosmetic outcomes in those taking oral treatment and no difference in negative outcomes.[18] Based on this, experts agree there is no evidence to support the delay of nonablative fractional devices and ablative fractional devices in patients who are receiving isotretinoin or have received isotretinoin in the last 6 months. Consensus remains that fully ablative (i.e., nonfractional) lasers should be postponed until at least 6 months post-treatment discontinuation.[6-8]

Laser Hair Removal

Several case series reporting uncomplicated laser hair removal (LHR) in patients receiving isotretinoin therapy for acne were first reported by Khatri and colleagues.[19-21] In these studies, 7, 6, and 11 patients on isotretinoin were treated with diode laser, intense pulsed light (IPL), and long-pulsed Nd:YAG laser, respectively. There were no reports of keloids or delayed wound healing. Similarly, another small case series of 6 patients on isotretinoin and treated with diode laser for hair removal reported cases of transient crusting, but no long-term negative sequelae or scar formation.[22] Two additional case series confirmed no negative outcomes with these procedures in patients taking isotretinoin.[10,15] Based on these data and expert consensus, there is insufficient evidence to delay LHR for patients actively taking or having recently completed isotretinoin therapy for acne.[6-7,23] Most recently, a retrospective study of 52 patients taking isotretinoin (10-50 mg/day) and receiving concomitant LHR with one of three devices (alexandrite, diode, and Nd:YAG lasers) were compared to a control group not on oral treatment for acne. Side effects were similar in both the isotretinoin and control groups with a few patients reporting temporary crusting and one patient in the isotretinoin group experiencing temporary hypopigmentation. There were no reports of hyperpigmentation, ulceration, blistering or scarring in either group.[24] Accordingly, there is no indication to delay laser hair removal in patients on or having recently completed isotretinoin therapy for acne.[6-8]

Microneedling and Dermaroller

There is a paucity of data on the use of microneedling in the context of oral isotretinoin use.[10,15] One study included only one microneedling patient. Following 7 sessions of therapy, post-inflammatory hyperpigmentation was noted which resolved without permanent sequelae.[10] In another study, 12 patients underwent treatment with a dermaroller device with only transient erythema and edema noted.[15] There were no patients reported to have experienced abnormal wound healing or scar formation in either study. Based on this information, the Association of Cutaneous Surgeons task force recommended that microneedling and dermaroller can be safely performed on patients with recent or concurrent isotretinoin administration.[8]

Radiofrequency Microneedling

In one study, 26 patients treated with radiofrequency microneedling for acne scarring were compared (13 on isotretinoin, and 13 without oral therapy). One case of hyperpigmentation occurred in each group and resolved over 6-8 weeks with the use of sunscreen, topical low-potency steroid cream, arbutin and kojic acid application.[15] More recently, a retrospective observational study was published looking at scar improvement in 71 patients treated with radiofrequency microneedling and fractional ablative laser. Importantly, 43 of these patients were receiving concomitant low-dose isotretinoin or had completed therapy within the previous 3 weeks. Combination treatment led to a significant improvement in acne scarring, as well as inflammatory acne lesions. Importantly, those on isotretinoin reported greater improvement in acne scarring, with no persistent side effects or abnormal scarring.[25] Based on this, the Association of Cutaneous Surgeons task force suggests that it is likely safe to treat superficial lesions with radiofrequency devices, but the task force still cautions that a 6-month delay for deeper lesions is warranted.[8]

Surgery

A large systematic review of patients undergoing elective surgical procedures while receiving isotretinoin was published in 2016. This review concluded that it was safe to operate on patients taking oral isotretinoin provided they were otherwise healthy and without abnormal pre-operative laboratory results.[26] A subsequent single-centre retrospective analysis compared the surgical outcomes of 203 acne patients exposed to isotretinoin in the peri-operative period (76 patients underwent surgery ≤ 2 years from the isotretinoin start date; 127 patients underwent surgery > 2 years from the isotretinoin start date) to 82 acne patients not exposed to isotretinoin. Surgical procedures all involved cutting of the skin and ranged from tonsillectomy and tooth extraction to double mastectomy. Wound healing was reported to be normal in both groups and without abnormal scarring.[27] As such, consensus recommendations do not support delaying cutaneous surgery for patients currently taking or having recently completed isotretinoin therapy, especially in those cases in which it is medically necessary.[6-7] In certain circumstances, avoidance of isotretinoin in the peri-operative period may still be warranted. The American Society for Dermatologic Surgery task force continues to recommend a 6-month delay post-isotretinoin therapy prior to performing LASIK eye surgery due to the increased risk of developing dry eye disease.[7]

Conclusion/Discussion

Despite the efficacy of oral isotretinoin in the management of acne, many patients are still left with scarring. Until recently, expert consensus has suggested a 6-month delay following treatment completion prior to the initiation of interventions for scar management and other cosmetic procedures. Recent published studies conclude that there is insufficient evidence to support this delay for many procedures including superficial chemical peels, focal or manual dermabrasion, and non-ablative lasers (**Table 1**). The adoption of recent consensus guidelines will allow patients access to effective interventions that can not only hasten acne resolution, but also safely address the debilitating scarring associated with this dermatologic condition.

Drop the 6-month procedural delay following isotretinoin therapy
Superficial chemical peels
Microdermabrasion
Focal or superficial manual dermabrasion
Fractional ablative and non-ablative lasers
Laser hair removal
Microneedling and radiofrequency microneedling
Cutaneous surgery*
Maintain the 6-month procedural delay following isotretinoin therapy
Medium and deep chemical peels
Full face dermabrasion or mechanical dermabrasion
Fully ablative (i.e., non-fractional) laser

*Surgical procedures should not be delayed especially when considered medically necessary; the ASDS Task Force still maintains a recommendation of a 6-month delay for LASIK eye surgery following isotretinoin therapy

Table 1: *New consensus recommendations regarding procedural delay following isotretinoin therapy; courtesy of Kim Blakely, MD, PhD*

References

1. *Hernandez-Perez E, Khawaja HA, Alvarez TY. Oral isotretinoin as part of the treatment of cutaneous aging. Dermatol Surg. 2000;26(7):649-652.*
2. *Picosse FR, Yarak S, Cabral NC, Bagatin E. Early chemabrasion for acne scars after treatment with oral isotretinoin. Dermatol Surg. 2012;38(9):1521-1526.*
3. *Kar BR, Tripathy S, Panda M. Comparative study of oral isotretinoin versus oral isotretinoin + 20% salicylic Acid peel in the treatment of active acne. J Cutan Aesthet Surg. 2013;6(4):204-208.*
4. *Chandrashekar BS, Vadlamudi SL, Shenoy C. Safety of Performing Superficial Chemical Peels in Patients on Oral Isotretinoin for Acne and Acne-Induced Pigmentation. J Clin Aesthet Dermatol. 2021;14(11):41-43.*
5. *Gerber PA, Kukova G, Bölke E, Homey B, Diedrichson E. Severe hyperpigmentation and scarring following glycolic acid peel treatment in combination with low-dose isotretinoin. Eur J Med Res. 2014;19(1):60.*
6. *Spring LK, Krakowski AC, Alam M, et al. Isotretinoin and Timing of Procedural Interventions: A Systematic Review With Consensus Recommendations. JAMA Dermatol. 2017;153(8):802-809.*
7. *Waldman A, Bolotin D, Arndt KA, et al. ASDS Guidelines Task Force: Consensus Recommendations Regarding the Safety of Lasers, Dermabrasion, Chemical Peels, Energy Devices, and Skin Surgery During and After Isotretinoin Use. Dermatol Surg. 2017;43(10):1249-1262.*
8. *Mysore V, Mahadevappa OH, Barua S, et al. Standard Guidelines of Care: Performing Procedures in Patients on or Recently Administered with Isotretinoin. J Cutan Aesthet Surg. 2017;10(4):186-194.*
9. *Bagatin E, dos Santos Guadanhim LR, Yarak S, Kamamoto CS, de Almeida FA. Dermabrasion for acne scars during treatment with oral isotretinoin. Dermatol Surg. 2010;36(4):483-489.*
10. *Mahadevappa OH, Mysore V, Viswanath V, et al. Surgical Outcome in Patients Taking Concomitant or Recent Intake of Oral Isotretinoin: A Multicentric Study-ISO-AIMS Study. J Cutan Aesthet Surg. 2016;9(2):106-114.*
11. *Roenigk HH Jr, Pinski JB, Robinson JK, Hanke CW. Acne, retinoids, and dermabrasion. J Dermatol Surg Oncol. 1985;11(4):396-398.*
12. *Rubenstein R, Roenigk HH Jr, Stegman SJ, Hanke CW. Atypical keloids after dermabrasion of patients taking isotretinoin. J Am Acad Dermatol. 1986;15(2 Pt 1):280-285.*
13. *Zachariae H. Delayed wound healing and keloid formation following argon laser treatment or dermabrasion during isotretinoin treatment. Br J Dermatol. 1988;118(5):703-706.*
14. *Katz BE, Mac Farlane DF. Atypical facial scarring after isotretinoin therapy in a patient with previous dermabrasion. J Am Acad Dermatol. 1994;30(5 Pt 2):852-853.*
15. *Chandrashekar BS, Varsha DV, Vasanth V, Jagadish P, Madura C, Rajashekar ML. Safety of performing invasive acne scar treatment and laser hair removal in patients on oral isotretinoin: a retrospective study of 110 patients. Int J Dermatol. 2014;53(10):1281-1285.*
16. *Kim HW, Chang SE, Kim JE, Ko JY, Ro YS. The safe delivery of fractional ablative carbon dioxide laser treatment for acne scars in Asian patients receiving oral isotretinoin. Dermatol Surg. 2014;40(12):1361-1366.*
17. *Leal H, Cantu P. Fractionated erbium laser during oral isotretinoin treatment. J Am Acad Dermatol 64:AB18.*
18. *Yoon JH, Park EJ, Kwon IH, et al. Concomitant use of an infrared fractional laser with low-dose isotretinoin for the treatment of acne and acne scars. J Dermatolog Treat. 2014;25(2):142-146.*
19. *Khatri KA. Diode laser hair removal in patients undergoing isotretinoin therapy. Dermatol Surg. 2004;30(9):1205-1207.*
20. *Khatri KA, Garcia V. Light-assisted hair removal in patients undergoing isotretinoin therapy. Dermatol Surg. 2006;32(6):875-877.*
21. *Khatri KA. The safety of long-pulsed Nd:YAG laser hair removal in skin types III-V patients during concomitant isotretinoin therapy. J Cosmet Laser Ther. 2009;11(1):56-60.*
22. *Cassano N, Arpaia N, Vena GA. Diode laser hair removal and isotretinoin therapy. Dermatol Surg. 2005;31(3):380-381.*
23. *Prather HB, Alam M, Poon E, Arndt KA, Dover JS. Laser Safety in Isotretinoin Use: A Survey of Expert Opinion and Practice. Dermatol Surg. 2017;43(3):357-363.*
24. *Sarigul Guduk S, Tukenmez Demirci G. Safety of Laser Hair Removal in Patients Receiving Systemic Isotretinoin for Acne Vulgaris. Dermatol Surg. 2021;47(11):1448-1452.*
25. *Kim J, Lee YI, Kim J, Jung JY, Lee WJ, Lee JH. Safety of Combined Fractional Microneedle Radiofrequency and CO2 as an Early Intervention for Inflammatory Acne and Scarring Treated With Concomitant Isotretinoin. Dermatol Surg. 2020;46(10):e71-e77.*
26. *Ungarelli LF, Hetem CM, Farina Junior JA. Is It Safe to Operate on Patients Taking Isotretinoin?. Aesthetic Plast Surg. 2016;40(1):139-148.*
27. *Tolkachjov SN, Sahoo A, Patel NG, Lohse CM, Murray JA, Tollefson MM. Surgical outcomes of patients on isotretinoin in the perioperative period: A single-center, retrospective analysis. J Am Acad Dermatol. 2017;77(1):159-161.*