International Journal of Otorhinolaryngology and Head and Neck Surgery
Mathews S et al. Int J Otorhinolaryngol Head Neck Surg. 2022 Sep;8(9):729-734
http://www.ijorl.com
pISSN 2454-5929 | eISSN 2454-5937
DOI: https://dx.doi.org/10.18203/issn.2454-5929.ijohns20222164

Original Research Article

Judicious management of pinna keloids: our experience with combination therapy

Sunil Mathews[1]*, Asha T. Jose[2], Varun Gangwar[1], Arumugam S. Vadivu[3], Raghu Nandhan[3]

[1]Department of ENT, INHS Sanjivani, Kochi, Kerala, India
[2]Department of Dermatology, St. Thomas Hospital, Chennai, Tamil Nadu, India
[3]Department of ENT, MERF, Chennai, Tamil Nadu, India

Received: 06 July 2022
Accepted: 30 July 2022

***Correspondence:**
Dr. Sunil Mathews,
E-mail: drsunilmathews@gmail.com

ABSTRACT

Background: Keloids occur as a result of overgrowth of fibrous tissue following healing of a cutaneous injury and they cause aesthetic issues when they appear on the exposed parts of the body, especially the face. Keloids are difficult to treat, with a high recurrence rate. There are several treatment modalities for management of keloids, though no single modality is completely effective. Most commonly used treatment modalities are intra-lesional steroids, surgical excision, pressure application, silicone gel sheets, 5-fluorouracil (5-FU), cryotherapy, radiation therapy, laser therapy or a combination of these modalities. The aim of the study was to analyse the causes of development of keloids on the pinna and evaluated the outcomes of various treatment modalities applied. It focused on assessing the clinical efficacy of combined surgical excision of pinna keloids with serial steroid injections to prevent recurrence, in comparison to monotherapy with intra-lesional steroid injections alone.
Methods: A retrospective review based on medical records was done for 18 patients with keloid of pinna, who were treated with either monotherapy or combination therapy.
Results: Satisfactory low recurrence rates were observed with meticulous surgical excision followed by serial steroid injections (18.2%), as compared to monotherapy with serial steroid injections alone (71.4%), and these comparative results were statistically significant at $p<0.05$ in the cohort.
Conclusions: A judicious plan for management for pinna keloids is necessary in order to achieve the best functional and cosmetic outcomes, while reducing the recurrence rates to a minimum. Following a combination of interventions has proved safe and effective for managing this challenging entity.

Keywords: Pinna, Keloid, Surgical excision, Steroid injection, Combined therapy, Recurrence

INTRODUCTION

In the natural wound healing process of the body, when there is an imbalance between anabolic and catabolic phases of scar formation, a pathologic scar can result. Keloid is one of such notorious pathologic scars, and the other is the milder variant of a hypertrophic scar. Unlike the hypertrophic scar wherein it stays within the original boundaries of scar, even if it continues to rise, keloid scar grows well beyond the initial wound boundaries. Although there are over 3000 years of history of keloids since the first description of keloid given by Smith Papyrus in 3000 BC, still, there is no perfect treatment available for this disease. Keloids arise mostly at puberty with peak age of onset between 10 and 30 years. The exact pathophysiology of keloid is not fully understood, but there are a number of hypotheses proposed, as given in Table 1.[1] Irrespective of these different hypotheses, the primary biochemical abnormality is the imbalance between matrix degradation and collagen synthesis, resulting in excess accumulation of dense collagen in the wound. Even though, the risk to develop keloid is equal between men and women, there is

a female predominance due to the number of ear lobe keloids developing in women secondary to ear lobe piercing.[2] In all ear piercings, the incidence of keloids is 2.5%.[3] There are a number of treatment options for keloids in world literature, which indicates that none of the treatment modality is very satisfactory in all patients and there is no universally accepted protocol yet. These lacunae in management protocol stimulated the need for this study. The objective of this study was to assess the effectiveness of combining surgical excision of keloids over pinna along with serial steroid injections at the excision site to prevent recurrence, in comparison to monotherapy with serial intra-lesional steroid injections alone.

Table 1: Proposed hypotheses on development of keloid.

Hypotheses	Proposed pathophysiology
Sebum autoimmune hypothesis	Keloids are a result of immune reaction to sebum, which acts as antigen, and is secreted intradermally following trauma. This is supported by the fact that humans are the only animals with sebaceous glands and true keloids develop only in humans.
Hypoxia hypothesis	It asserts that hypoxia present in keloid stimulate excessive collagen production.
Tension hypothesis	Keloids are caused by excessive tension in wounds.
Hormonal hypothesis	It is supported by the occurrence of keloids at puberty and pregnancy, worsening during pregnancy and rarity in postmenopausal women. Keloid scars demonstrate higher level of androgen binding than surrounding normal tissue.
Essential fatty acid hypothesis	An essential fatty acid precursor deficiency and inflammatory competitors for arachidonic acid may be a factor for keloid formation.

METHODS

This work was a clinical audit of outcomes based on retrospective data collected from medical records of patients visiting the otorhinolaryngology department at a zonal level naval hospital. 18 patients who underwent treatment between January 2017 to December 2018 and who had subsequent minimum follow up of 1 year were selected. Ethical clearance was obtained from the institute as needed. Pregnant and lactating mothers, patients with concomitant illnesses like renal failure, hepatic diseases, acid peptic disease and hypertension were all excluded from this study, as steroid injection was not advisable for them. All included patients were explained about the two treatment options we offered, as both were considered as standard treatments. The patients as per their logistics and wishes did the choice of treatment. Informed consent was taken prior to each intervention.

Surgical excision alone was not offered to any patient due to the high recurrence rates known in literature. A total of 18 keloids of pinna were treated over a two year period. Patients were divided into 2 groups: group A had 7 keloids who received only steroid injections (Table 2), and group B had 11 keloids who were treated with surgical excision with intra-operative and post-operative steroid injections (Table 3). There was no crossover of patients from group A to group B. In all these patients, the lesion was extending well beyond the boundaries of initial site of ear piercing, thus confirming a clinical diagnosis of keloid and differentiating it from hypertrophic scar. All keloids were surgically excised and/or given steroid injections by the same surgeon in the same surgical settings. Cold-steel instruments were preferred for surgical excision. Local infiltration was given with 2% lignocaine without adrenaline. Number 15 blade on a Bard Parker handle along with sharp tissue cutting scissors and toothed forceps were used for dissection (Figure 1). Bipolar cautery was sparingly used only for bleeders which were not controlled with digital pressure. First intralesional steroid injection was given after surgical excision into the bed before suturing (Figure 2). Wounds were closed in a single layer with mattress sutures with 5-0 prolene and sutures were removed on the 14th post-op day. The excised specimen was sent for histopathological examination and the diagnosis of keloid was confirmed (Figure 3). Post operatively antibiotic ointment was applied on the wound for three weeks. Pressure therapy, silicone sheet/gel application and moisturizing agents were not used in the post-operative management of scars.

For every keloid, a total of five injections were given, at three weekly intervals onto the scar (0, 3, 6, 9 and 12 weeks) using a 2 ml syringe with 26G needle. Triamcinolone acetonide 40 mg/ml was used for injection, depending on the size and dose required to inject. Dose to be injected was calculated based on length multiplied by breadth of the keloid (for initial injection per-operatively)/dimensions of scar (for subsequent injections during follow up following surgical excision), multiplied by 5 mg. For the monotherapy group also, five injections were given on 0, 3, 6, 9 and 12 weeks, as per the same dose calculation for the keloid size at the time of injection. Recurrence was noted as growth in the scar tissue with increasing thickness in the scar or surrounding tissue distortion, compared to the size of scar at suture removal. Response to monotherapy with serial steroid injections was noted as at least 50% reduction in size of keloid with no recurrence in one-year follow up. All female patients were instructed to avoid future ear piercings. All patients were followed up for a minimum period of 1 year and the results were analyzed and outcomes compared statistically between the two groups. The descriptive data were interpreted in percentages and for continuous data, the mean was determined. Post-treatment outcome comparison between the groups, was done with Fisher's

exact test using eZR software by biostatistician and appropriate inferences were derived as shown in Table 4.

RESULTS

The main presenting complaint of all pinna keloids was cosmetic deformity, with only two patients complaining of pruritus and one patient complained of pain, in addition to cosmetic deformity. In 100% of female patients, the etiology was ear piercing. A single case of male keloid was developed following a minor trauma to the ear. In group A, 100% were females with an average age of 32.4 years (range- 25 to 41 years) and in group B, 90.9% were females with an average age of 37.6 years (range- 24 to 54 years). Most of the keloids of pinna developed on the ear lobe- 85% in group A and in 82% in group B. All the keloids were either reniform or bulbous shape. The pre- and post- treatment (combination therapy) comparison of an ear lobe keloid is represented in Figure 4.

Hyperpigmentation of the skin was the most commonly seen side effect which was seen in 57% in group A and 63.6% in group B (Figure 5). The other undesired effect seen in our cohort, was a wedge defect at the surgical excision site in one patient in group B, on completion of steroid injections, which required a cosmetic ear lobe repair later on. Satisfactory low recurrence rates were observed with meticulous surgical excision followed by serial steroid injections (18.2%), as compared to monotherapy with serial steroid injections alone (71.4%), and these comparative results were statistically significant at $p<0.05$ in the cohort.

Table 2: Patients treated with monotherapy of serial injections of steroid (group A).

S. no.	Age (years)	Gender	Site	Side	Length×breadth (cm)	Etiology	Recurrence/ no reduction in size	Side effects
1.	30	F	Ear lobe	RT	1×1	Ear piercing	Yes	Nil
2.	32	F	Helix	RT	1.5×1.5	Ear piercing	Yes	Hyperpigmentation
3.	36	F	Ear lobe	RT	1.5×1	Ear piercing	Yes	Nil
4.	28	F	Ear lobe	RT	1×1	Ear piercing	No	Hyperpigmentation
5.	41	F	Ear lobe	LT	2×1.5	Ear piercing	Yes	Nil
6.	25	F	Ear lobe	RT	1×0.5	Ear piercing	No	Hyperpigmentation
7.	35	F	Ear lobe	RT	2×1	Ear piercing	Yes	Hyperpigmentation

Table 3: Patients treated with combination therapy of surgical excision and intra operative and post-operative serial injections of steroid (group B).

S. no.	Age (years)	Gender	Site	Side	Length×breadth (cm)	Etiology	Recurrence	Side effects
1.	36	F	Ear lobe	RT	3×2	Ear piercing	No	Hyperpigmentation
2.	30	F	Ear lobe	LT	4×3	Ear piercing	Yes	No
3.	32	F	Helix	RT	2×1	Ear piercing	No	Hyperpigmentation
4.	47	F	Ear lobe	LT	3.5×3	Ear piercing	No	Hyperpigmentation
5.	45	F	Helix	LT	2×2	Ear piercing	No	No
6.	41	F	Ear lobe	RT	3×2	Ear piercing	No	Hyperpigmentation
7.	54	F	Ear lobe	RT	2.5×2	Ear piercing	No	Hyperpigmentation and wedge deformity at excision site
8.	42	M	Ear lobe	LT	2×1.5	Following ear trauma	No	No
9.	29	F	Ear lobe	RT	3×2	Ear piercing	No	Hyperpigmentation

Continued.

S. no.	Age (years)	Gender	Site	Side	Length×breadth (cm)	Etiology	Recurrence	Side effects
10.	24	F	Ear lobe	RT	2×2	Ear piercing	Yes	No
11.	38	F	Ear lobe	RT	2.5×2	Ear piercing	No	Hyperpigmentation

Table 4: Statistical analysis using Fisher's exact test.

Fisher's exact test comparing recurrence rates of monotherapy and combination therapy	Only steroid injection	Surgery and steroid injection	Row totals
No recurrence	2 (28.6%)	9 (81.8%)	11
Recurrence/ no reduction in size	5 (71.4%)	2 (18.2%)	7
Column totals	7	11	18 (Grand total)

Note: p value is 0.049 and is significant at $p<0.05$.

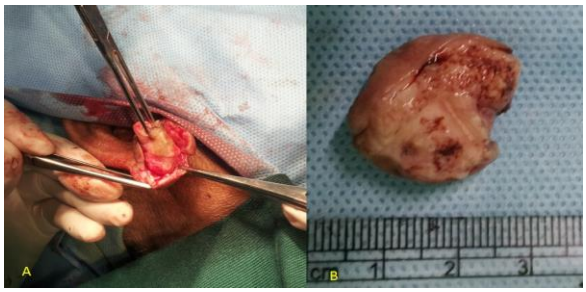

Figure 1: Surgical excision of keloid on ear lobe (A) surgical excision; and (B) excised specimen of keloid.

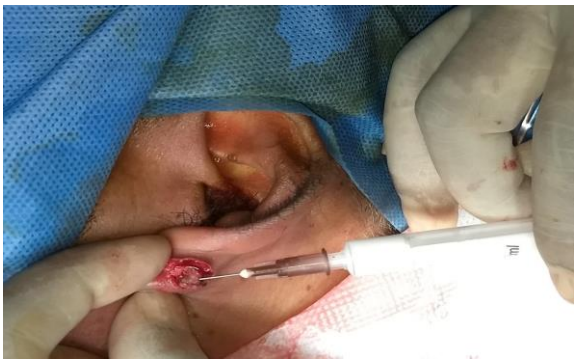

Figure 2: Steroid injection into the surgical bed after excision of keloid.

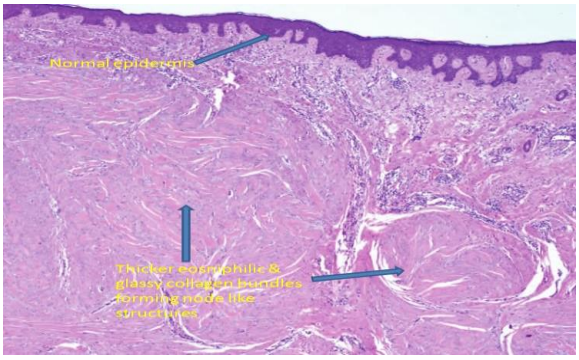

Figure 3: Histopathological confirmation of keloid.

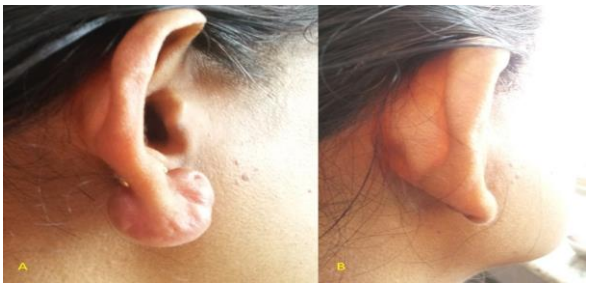

Figure 4: Example of a pre and post-operative comparison of keloid pinna without recurrence (A) pre-operative presentation of a case of keloid of ear lobe; and (B) six months after surgical excision and serial steroid injections.

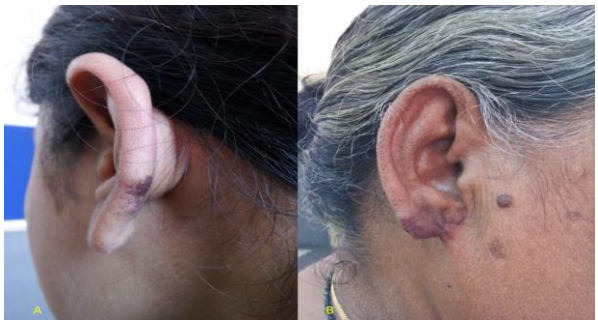

Figure 5: Hyperpigmentation - the most common side effect noted after serial steroid injections following surgical excision (A) hyper pigmentation of helical margin; and (B) hyper pigmentation of ear lobe.

DISCUSSION

Trauma is the main provoking factor in most patients and it can occur in the form of abrasions, incisions, ear piercing, insect bites, chemical or thermal burns, acne, chicken pox and bacterial or viral infections. In keloidal fibroblasts, the negative feedback mechanism is somehow defective, resulting in exuberant scar, which has the propensity to recur.[4]

The keloidal fibroblasts have shown to over express the growth factors: vascular endothelial growth factor (VEGF), transforming growth factors (TGF) β1 and β2, connective tissue growth factor (CTGF) and platelet derived growth factor PDGF-α receptor.[5] It is known that TGF- β1 and β2 are profibrotic and promote scar formation. Keloids on histopathology show a normal epidermal layer and thickened dermis. They have thicker, more eosinophilic and glassy collagen bundles which are closely arranged and more abundant, yielding acellular, node like structures in the deep dermis. Similar to collagen, proteoglycans are another major extra cellular matrix component secreted in excess amounts and, there is a decreased concentration of adnexal structures in the keloid scars.[6]

Various treatment modalities described in literature for keloids are surgical excision, intralesional injection with corticosteroids, cryotherapy, laser therapy, pressure therapy, silicone material application, radiotherapy, 5-flourouracil (5-FU), bleomycin, imiquimod, and combinations of these methods.[1,3] Surgical excision when performed alone may lead to a high recurrence rate between 50-100%.[7] So, in general, excision alone is not preferred for keloids. Corticosteroids are the most commonly used treatment modality, most commonly used being triamcinolone acetonide due to its potency to work on collagen and prolonged action. In keloids, this is given at a dose of 40 mg/ml. It acts by the suppression of inflammation by inhibition of migration of leukocytes and monocytes, and phagocytosis; vasoconstriction leading to hypoxia and antimitotic effect inhibiting keratinocytes and fibroblast proliferation. It also causes enhanced collagen and fibroblast degeneration.[8]

Rosen and colleagues treated ear keloids with surgical excision and intra-operative and post-operative injections of steroid and reported a recurrence rate of 23%.[9] De Sousa and colleagues excised 22 pinna keloids in 10 patients, with intra operative and post-operative serial triamcinolone acetonide injections (3, 6, 9 and 12 weeks) at a dose of 10 mg/cm^2 and silicone sheet application (started at 3 weeks post-operatively) for 12 hours per night for 3 months. They observed a recurrence of two keloids after one year of follow up (recurrence rate of 9.1%).[3] In a recent meta-analysis of 25 studies, a recurrence rate of 15.4% was seen for surgery followed by triamcinolone acetonide injections.[10] A similar response of 18% recurrence was noted in our present study, with combination therapy using surgical excision with intra-operative and post-operative steroid injections.

Intra-lesional injection of corticosteroids alone when used as a first line therapy, is known to respond in 50 to 100% of cases and its recurrence rates are between 9 to 50%.[1] In the present study we have observed a higher rate (70%) of recurrence/ no response to periodic (three weekly) intra-lesional triamcinolone acetonide injections, which negates the use of single modality therapy as a treatment of choice for pinna keloids. Side effects of intra-lesional corticosteroid injections noted in literature are hypo- or hyper-pigmentation, telangiectasia, skin atrophy, ulceration, gastritis and pain upon injection.[3,11] Silicone material is available in the form of creams, gel sheets and silastic sheets. Although the mechanism of action is poorly understood, silicone is thought to affect hydration of the skin by decreasing water vapour transmission rate, which is responsible for decrease in capillary permeability, reduced hyperaemia and reduced collagen deposition. Pressure therapy is known to be effective when it is above the arterial capillary closing pressure of 25 mm of Hg. The recommendation is that pressure on the lesion should be around 20 to 40 mm of Hg, but not above 40 mm of Hg, to avoid reduction in peripheral circulation.[1]

In a recent study evaluating multimodal approach to keloids, surgical excision followed by betamethasone injections and pressure therapy using custom made magnets achieved a cure rate of 87.2%.[12] According to Ogawa and colleagues, the dosage of radiotherapy for ear lobe is 10 Gray (Gy) in two fractions over two days, and the radiotherapy can start from first or second day after surgery.[13] In a recent study on 35 keloids managed with surgical excision followed by radiation therapy, seven recurred, giving a recurrence rate of 20%.[14] 5-FU when given as an intralesional therapy blocks collagen synthesis, inhibits fibroblast proliferation and also has an inhibitory effect on transforming growth factor-β (TGF-β) induced type I collagen gene expression in human fibroblasts.[15] Bleomycin acts by inhibiting DNA, RNA and protein synthesis as well as by inducing apoptosis. It has to be administered either by intradermal injections or by multiple punctures into the keloid.[16] Imiquimod cream application inhibits collagen production by release of interferon- α and ɣ, which alter expression of apoptotic gene, which is important for the expression of this disease.[1] To summarize this study, all patients except one, with keloid of pinna in this study were females in their third to sixth decade of life and in all female patients, ear piercing was the predisposing cause. Serial steroid injections given as the first line therapy for keloids, produced high recurrence/ no response to treatment in this study in 70% of the cases. Combination therapy with surgical excision followed by serial steroid injections gave better results with low recurrence rates (18% only). The main side effect observed with steroid injection was hyperpigmentation of the skin in 60% cases.

Strengths

All procedures and follow up were carried out by the same surgeon, and pre-operative and follow up data of all patients were available for the study.

Limitations

The sample size in our study was less and follow up duration was relatively shorter due to the transfer of patients in a naval establishment set up. In addition, due to the institutional protocols, there was inability to explore

other treatment options like radiation therapy/laser therapy/cryotherapy/5-FU/bleomycin etc for comparison. A prospective multimodality long term clinical trial including these above arms has been proposed for a future study at our institution.

CONCLUSION

A judicious plan for management for pinna keloids is necessary in order to achieve the best functional and cosmetic outcomes, while reducing the recurrence rates to a minimum. In our experience, following a combination of interventions such as surgical excision along with serial steroid injections, has proved safe and effective for managing this challenging entity.

Recommendations

Exciting research work is currently underway in this realm with human skin grafting on athymic mice and porcine models, which should help in better understanding of the pathogenesis of keloid formation and in devising better treatment options in the near future. Current research is focussing on therapeutic modalities including surface brachytherapy, monoclonal antibodies and platelet rich plasma therapy, all of which are showing promising early results with long term outcomes awaited.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Varma S, Gupta S. Keloid and hypertrophic scar. In: Venkataram M, eds. Textbook on Cutaneous and Aesthetic Surgery. 1st ed. New Delhi: Jaypee Brothers Medical Publishers; 2012: 498-513.
2. Bayat A, Arscott G, Ollier WE, McGrouther DA, Ferguson MW. Keloid disease: clinical relevance of single versus multiple site scars. Br J Plast Surg. 2005;58(1):28-37.
3. Sousa RF, Chakravarty B, Sharma A, Parwaz MA, Malik A. Efficacy of triple therapy in auricular keloids. J Cutan Aesthet Surg. 2014;7(2):98-102.
4. Robles DT, Moore E, Draznin M, Berg D. Keloids: pathophysiology and management. Dermatol Online J. 2007;13(3):9.
5. Marneros AG, Krieg T. Keloids--clinical diagnosis, pathogenesis, and treatment options. J Dtsch Dermatol Ges. 2004;2(11):905-13.
6. Ogawa R, Akaishi S, Izumi M. Histologic analysis of keloids and hypertrophic scars. Ann Plast Surg. 2009;62(1):104-5.
7. Nast A, Eming S, Fluhr J, Fritz K, Gauglitz G, Hohenleutner S, et al. German S2k guidelines for the therapy of pathological scars (hypertrophic scars and keloids). J Dtsch Dermatol Ges. 2012;10(10):747-62.
8. Reish RG, Eriksson E. Scar treatments: preclinical and clinical studies. J Am Coll Surg. 2008;206(4):719-30.
9. Rosen DJ, Patel MK, Freeman K, Weiss PR. A primary protocol for the management of ear keloids: results of excision combined with intraoperative and postoperative steroid injections. Plast Reconstr Surg. 2007;120(5):1395-400.
10. Shin JY, Lee JW, Roh SG, Lee NH, Yang KM. A Comparison of the Effectiveness of Triamcinolone and Radiation Therapy for Ear Keloids after Surgical Excision: A Systematic Review and Meta-Analysis. Plast Reconstr Surg. 2016;137(6):1718-25.
11. Gupta S, Sharma VK. Standard guidelines of care: Keloids and hypertrophic scars. Indian J Dermatol Venereol Leprol. 2011;77(1):94-100.
12. Hao YH, Xing XJ, Zhao ZG, Xie F, Hao T, Yang Y, et al. A multimodal therapeutic approach improves the clinical outcome of auricular keloid patients. Int J Dermatol. 2019;58(6):745-9.
13. Ogawa R, Miyashita T, Hyakusoku H, Akaishi S, Kuribayashi S, Tateno A. Postoperative radiation protocol for keloids and hypertrophic scars: statistical analysis of 370 sites followed for over 18 months. Ann Plast Surg. 2007;59(6):688-91.
14. Lyu A, Xu E, Wang Q. A retrospective analysis of surgical resection of large ear keloids. Australas J Dermatol. 2019;60(1):29-32.
15. Asilian A, Darougheh A, Shariati F. New combination of triamcinolone, 5-Fluorouracil, and pulsed-dye laser for treatment of keloid and hypertrophic scars. Dermatol Surg. 2006;32(7):907-15.
16. Yamamoto T. Bleomycin and the skin. Br J Dermatol. 2006;155(5):869-75.

Cite this article as: Mathews S, Jose AT, Gangwar V, Vadivu AS, Nandhan R. Judicious management of pinna keloids: our experience with combination therapy. Int J Otorhinolaryngol Head Neck Surg 2022;8:729-34.