การเปรียบเทียบประสิทธิภาพและการกลับเป็นซ้ำของการฉีดยาเวอราปามิล และยาไตรแอมซิโนโลนเข้าในรอยโรคสำหรับการรักษาคีลอยด์ที่หูหลังการผ่าตัด: การทดลองแบบสุ่มที่มีกลุ่มควบคุม

สุมิตรา จันทร์เพ็ง
กลุ่มงานศัลยกรรม ศูนย์แพทยศาสตรศึกษาชั้นคลินิก โรงพยาบาลชัยภูมิ

Received: July 27, 2024
Revised: August 25, 2024
Accepted: August 26, 2024

บทคัดย่อ

คีลอยด์เป็นแผลเป็นนูนนอกขอบเขตแผลเดิม เกิดจากกระบวนการหายของแผลที่มีการสร้างหรือซ่อมแซมมากเกินไป ปัจจุบันยังไม่มีวิธีการรักษาคีลอยด์โดยการรักษาด้วยวิธีเดียวอย่างมีประสิทธิภาพ การรักษาด้วยการผ่าตัดมีโอกาสกลับมาเป็นซ้ำสูงถึงร้อยละ 45 ถึง 100 การผ่าตัดร่วมกับการฉีดยาสเตียรอยด์สามารถลดโอกาสการกลับมาเป็นซ้ำได้สูง ปัจจุบันเวอราปามิลเป็นอีกทางเลือกหนึ่งในการรักษาคีลอยด์ตามคำแนะนำของ European guidelines เนื่องจากสามารถลดขนาดและรักษาคีลอยด์ให้ดีขึ้น อีกทั้งยังเกิดผลข้างเคียงน้อย การศึกษาวิจัยทางคลินิกนี้ได้ศึกษาถึงประสิทธิภาพของยาสองชนิดในการรักษาคีลอยด์ที่หูหลังการผ่าตัด โดยมีผู้ป่วยจำนวน 52 รายเข้าได้กับเกณฑ์การคัดเข้า ได้รับการผ่าตัดคีลอยด์ที่หู โดยแบ่งเป็นสองกลุ่ม กลุ่มที่ 1 จำนวน 26 คน ได้รับการฉีดยาไตรแอมซิโนโลนเข้าในรอยโรค กลุ่มที่สอง จำนวน 26 คน ได้รับการฉีดยาเวอราปามิลเข้าในรอยโรค โดยฉีดยา 2 ครั้ง ครั้งแรกหลังการผ่าตัดทันที ครั้งที่สองห่างจากครั้งแรก 4 สัปดาห์ จากนั้นตรวจติดตามทุก 8 สัปดาห์ จนครบ 1 ปี ผลการศึกษาพบการกลับมาเป็นซ้ำของคีลอยด์ที่หูในทั้งสองกลุ่ม โดยกลุ่มที่ได้รับยาไตรแอมซิโนโลน พบ 4 คน (ร้อยละ 15.4) ส่วนกลุ่มที่ได้รับยาเวอราปามิล พบ 6 คน (ร้อยละ 23.1) หลังการผ่าตัด 44 สัปดาห์ ผู้ป่วยทั้งสองกลุ่มมีการเปลี่ยนแปลงของ Vancouver Scar Scale (VSS) scores อย่างมีนัยสำคัญทางสถิติ แต่ในกลุ่มที่ได้รับยาไตรแอมซิโนโลนพบว่าสีของแผลเป็น ความยืดหยุ่น และผลรวมของ VSS scores มีผลลัพธ์ที่ดีขึ้นเร็วกว่าในกลุ่มที่ได้รับยาเวอราปามิล ส่วนรอยดำ รอยด่าง กลุ่มที่ได้รับยาเวอราปามิลมีผลลัพธ์ที่ดีขึ้นเร็วกว่าในกลุ่มที่ได้รับยาไตรแอมซิโนโลน ภาวะแทรกซ้อนพบว่ากลุ่มที่ได้รับยาไตรแอมซิโนโลนมีภาวะแทรกซ้อนมากกว่าอย่างมีนัยสำคัญทางสถิติ คือ เส้นเลือดฝอยโป่งพองและผิวหนังบางบริเวณที่ได้รับการฉีดยา โดยสรุป การฉีดยาเวอราปามิลเข้าในรอยโรคหลังการผ่าตัดคีลอยด์ที่หูมีประสิทธิภาพและไม่ด้อยไปกว่าการฉีดยาไตรแอมซิโนโลนเข้าในรอยโรค และยังพบภาวะแทรกซ้อนน้อยกว่า

คำสำคัญ: คีลอยด์ที่หู; การผ่าตัดคีลอยด์ที่หู; ไตรแอมซิโนโลน; เวอราปามิล; การฉีดยาเข้าในรอยโรค

ผู้นิพนธ์ประสานงาน:
สุมิตรา จันทร์เพ็ง
กลุ่มงานศัลยกรรม ศูนย์แพทยศาสตรศึกษาชั้นคลินิก โรงพยาบาลชัยภูมิ
12 ถนนบรรณาการ ตำบลในเมือง อำเภอเมืองชัยภูมิ จังหวัดชัยภูมิ 36000
อีเมล: little.sumatit@gmail.com

Comparison of efficacy and recurrence of intralesional Verapamil and Triamcinolone injection for postoperative ear keloid treatment: A randomized controlled trial

Sumitra Chanpeng
Surgery Department, Chaiyaphum Hospital Medical Education Center

Abstract

Keloids are abnormal scars caused by excessive and uncontrolled repair processes that extend beyond the original wound boundary. Currently, there is no single effective treatment modality for keloids, and surgical removal has a recurrence rate of 45% to 100%. Multimodality therapy, which combines steroid injections with surgery, can decrease recurrence rates. Verapamil is now recommended as an alternative treatment for keloids in European guidelines due to its ability to improve keloid appearance by reducing and modifying the scar, with minimal adverse effects. This clinical trial investigated the efficacy of two treatment methods for ear keloid excision. Fifty-two patients who met the inclusion criteria underwent ear keloid excision and were divided into two groups: 26 patients received an intralesional triamcinolone injection (Group T), and 26 patients received an intralesional verapamil injection (Group V). The injections were administered twice, immediately after surgical excision and then repeated 4 weeks later. Patients were followed up every 8 weeks for one year. The results showed that at 44 weeks after surgery, the recurrence of ear keloid scars was observed in 4 patients (15.4%) in Group T and 6 patients (23.1%) in Group V. Both groups demonstrated statistically significant improvements in Vancouver Scar Scale (VSS) scores. Group T experienced quicker resolution of skin redness or vascularity, pliability, and total VSS scores, while pigmentation showed a faster response in Group V. Group T also had significantly more complications, such as telangiectasia and dermal atrophy, compared to Group V. In conclusion, intralesional verapamil injection after ear keloid excision was found to be an effective and non-inferior treatment compared to intralesional triamcinolone injection, resulting in reduced post-treatment complications.

Keywords: ear keloid; ear keloid excision; Triamcinolone; Verapamil; intralesional injection

Corresponding Author:
Sumitra Chanpeng
Surgery Department, Chaiyaphum Hospital Medical Education Center
12 Bannakarn Road, Nai Muang Sub-district, Muang Chaiyaphum District, Chaiyaphum 36000, Thailand
E-mail: little.sumatit@gmail.com

Introduction

Wound healing is a normal physiological process that occurs when the body is injured. However, excessive healing can lead to undesirable conditions such as keloids and hypertrophic scars. Factors contributing to keloid formation include genetic predisposition, ethnicity, wound tension, hormonal status during pregnancy and puberty, and environmental factors. A study conducted on patients of Afro-Caribbean descent showed that more than 50% of the individuals with keloids had a positive family history[1]. Africans are up to 15 times more likely to develop keloids than Europeans[2]. Keloids typically occur between 10 and 30 years of age, with both males and females equally affected[3]. Keloids located on the ears, face, and neck are prominently visible, affecting appearance and reducing confidence levels. The medical profession has no agreed gold standard of therapy, and multimodality treatments have been developed to minimize the recurrence of keloids by combining surgical excision with different medications. Other treatment methods include pulsed dye laser, interferon alfa-2b, and cultured epithelial autografts[4]. Currently, one widely accepted and commonly used treatment for this condition is an intralesional triamcinolone acetonide (TA) injection[5,6], which inhibits the proliferation of keratinocytes and reduces fibroblast activity, consequently decreasing collagen production and leading to a reduction in keloid height. Verapamil is a Ca^{2+} channel blocker that has demonstrated promising results in the treatment of keloids by stimulating the production of collagenases that break down collagen, the major component of scars. Verapamil decreases the production of scar formation factors such as Interleukin-6 and Vascular Endothelial Growth Factor (VEGF), while also inhibiting the proliferation of fibroblasts and promoting the apoptosis of scar cells. These effects contribute to reducing and modifying keloids, making verapamil a valuable option for keloid treatment. Verapamil has fewer side effects compared to TA injection and shows promise for use in cases where corticosteroids are unsuitable[7,8,9].

Objective

To study the outcomes of treating ear keloids with intralesional TA injections compared to verapamil injections after excision.

Material and methods

This randomized controlled trial (RCT) was performed in accordance with the Declaration of Helsinki and the protocol was approved by the Research Ethics Committee (REC) of Chaiyaphum Hospital, reference No.006/2565.

Population and sample size: The sample population included patients who registered for keloid treatment at the Plastic Surgery Department, Chaiyaphum Hospital between March 2022 and March 2023.

The sample size was determined using a power analysis with an effect size of 0.50, based on the previous study[10]. The test power

(1-β) was set at 0.80, and the significance level (α) was set at 0.05. Using the G*Power program, the required sample size was calculated to be 26 participants per group.

The inclusion criteria for this research were:

1. Patients of both genders, aged between 14 and 70

2. Patients diagnosed with an ear keloid who underwent keloid excision by a plastic surgeon (one keloid per patient)

The exclusion criteria were as follows:

1. Patients with wounds, infection, inflammation, and skin tumor proximal to the ear keloid

2. Previous keloid treatments such as intralesional injection, surgery, silicone gel, or silicone sheet

3. Pregnancy or lactation

4. Diabetes mellitus, hypertension, cardiovascular disease, chronic kidney disease

5. Use of triamcinolone acetonide and/or verapamil for other medical conditions

6. A known history of allergy to steroids and/or verapamil

Fifty-two patients met the criteria. All provided informed consent. Simple random sampling was used to divide them into two groups (T and V), with allocation and concealment methods applied to prevent bias. The ear keloid excision was performed under local anesthesia using 1% lidocaine and 1:100,000 epinephrine. An incision was made around the edge of the keloid and the fibrous keloid core was completely removed. All the wounds were closed by the interrupted suture technique using one layer of 5-0 Ethilon without tension, with stitches removed 2 weeks after surgery. Two post-operative intralesional injections were given, with the first immediately after surgery and the second after 4 weeks. The patients in group T (control group) received TA (40 mg/ml) injections using an insulin syringe with a 25-gauge needle, injected at a rate of 0.1 ml for every 1 cm depending on the size of the surgical scar. Follow-up checks were conducted every 8 weeks for one year. Patients in group V (experimental group) received post-operative verapamil (2.5 mg/ml) injections following the same technique.

Assessment and outcome measurements

The patient data recording form was divided into two parts:

Part 1: Basic characteristics including gender, age, family history of keloid scars, duration of keloid formation, keloid anatomic location on the ear, side, etiology and volume. The volume of the keloid was measured using calipers.

Part 2: Treatment outcomes including primary outcome recurrence, defined as any indurated papule or nodule growing beyond the previous surgical scar boundaries. Secondary outcomes as scars were assessed by the Vancouver Scar Scale (VSS) as pigmentation, vascularity, pliability, height (Table 1) and complications of pain, telangiectasia, and dermal atrophy.

A quality assessment of the research tools was conducted by three qualified individuals. Content validity was assessed by

calculating the Item-Objective Congruence (IOC) index value and the congruence coefficient; the IOC was 0.78. The reliability was assessed at 0.81 using the Cronbach's alpha coefficient. Data analysis was conducted using SPSS software version 17.0, with descriptive statistics such as frequencies, percentages, means, and standard deviations also analyzed. Basic data comparisons between the experimental and control groups were performed using the Chi-square test and the independent T-test, while treatment outcomes as recurrence and complications between the experimental and control groups were performed using the Chi-square test and Fisher's exact test. The VSS scores were compared both within and between the two groups using the independent T-test. All *p*-values were two-tailed, with a value < 0.05 considered statistically significant.

Table 1 Vancouver Scar Scale (VSS) score[11]

Scar characteristic		Score
Vascularity	Normal	0
	Pink	1
	Red	2
	Purple	3
Pigmentation	Normal	0
	Hypopigmentation	1
	Hyperpigmentation	2
Pliability	Normal	0
	Supple: flexible with minimal resistance	1
	Yielding: giving way to pressure	2
	Firm: inflexible, not easily moved, resistant to manual pressure	3
	Ropes: rope-like tissue that branches with extension of the scar	4
	Contracture: permanent shortening of the scar, producing deformity or distortion	5
Height	Flat	0
	<2 mm	1
	2-5 mm	2
	>5 mm	3
Total score		13

Results

Most patients with an ear keloid who underwent surgery in both groups were female, comprising 88.5% in group T and 80.7% in group V. Average age was 22.81±10.45 years in group T and 21.23±4.22 years in group V. A positive family history of keloids was recorded by 7 patients (26.9%) in group T and 6 patients (23.1%) in group V. The average duration of keloid formation was 1.16±0.39 years and 1.18±0.28 years in groups T and V, respectively. The most common keloid

location was on the helix in both groups, followed by the anterior and posterior lobules (Figure 1). Keloids were more prevalent on the left than on the right side in both groups. The main cause of keloids was ear piercing. The average volume of keloids was 8.59±6.83 cm^3 in group T and 9.21±21.51 cm^3 in group V. The basic characteristic of the study populations showed no statistically significant differences (p>0.05) between the two groups (Table 2).

Table 2 Baseline characteristics of the study population

Basic characteristics	Triamcinolone (n=26) (%)	Verapamil (n=26) (%)	*p*-value
Gender			
Male	3 (11.5)	5 (19.3)	0.352
Female	23 (88.5)	21 (80.7)	
Age (years)			
< 16	1 (3.8)	1 (3.8)	0.348
16-20	4 (15.4)	5 (19.2)	
21-25	8 (30.8)	9 (34.6)	
26-30	10 (38.5)	8 (30.8)	
> 30	3 (11.5)	3 (11.5)	
Mean ± SD (min-max)	22.81 ± 10.45 (16-70)	21.23 ± 4.22 (16-33)	0.197
Family history of keloids	7 (26.9)	6 (23.1)	0.500
Duration of keloid formation (years, mean ± SD)	1.16 ± 0.39	1.18 ± 0.28	0.259
Anatomical location			
Helix	16 (61.5)	19 (73.1)	0.414
Anterior lobule	7 (26.9)	3 (11.5)	
Posterior lobule	3 (11.5)	3 (11.5)	
Post-auricular area	0 (0)	1 (3.8)	
Side			
Left	14 (53.8)	16 (61.5)	0.779
Right	12 (46.2)	10 (38.5)	
Etiology			
Trauma	1 (3.8)	1 (3.8)	0.390
Infection	2 (7.7)	1 (3.8)	
Ear piercing	23 (88.5)	23 (88.5)	
Surgical scar	0 (0)	1 (3.8)	
Volume (cm^3)	8.59 ± 6.83	9.21 ± 21.51	0.074

The primary outcome of the recurrence rate of ear keloid was not significantly different between both groups, with 4 patients (15.4%) in group T and 6 patients (23.1%) in group V recording keloid recurrence at the 44 week follow-up, as shown in Table 3.

A pre-operative keloid and the result after the one-year surgical follow-up without recurrence are shown in Figure 2, with keloid recurrence 44 weeks after surgery shown in Figure 3.

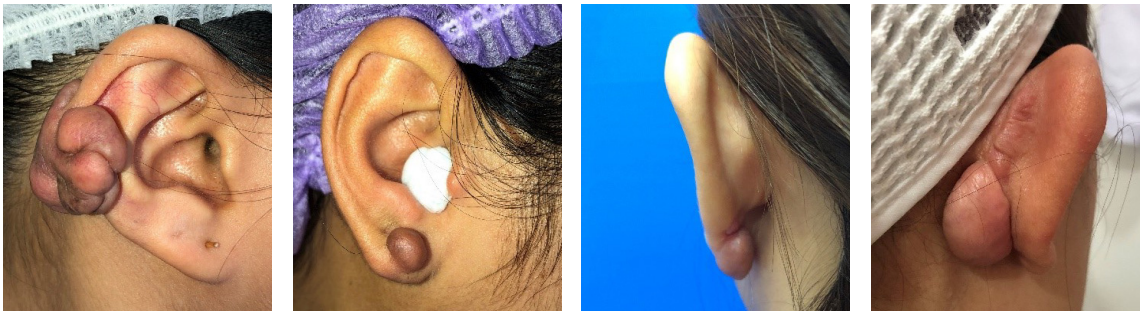
Secondary outcomes as complications of pain after injection, telangiectasia, and dermal atrophy were recorded in 24 (92.4%), 3 (11.5%), and 7 (26.9%) of patients in group T, respectively. Twenty-three patients (88.5%) experienced pain after injection in group V but no telangiectasia and dermal atrophy were observed, with results shown in Table 3.

Table 3 Treatment outcomes compared between the triamcinolone and verapamil groups

Outcome	Triamcinolone (n=26) (%)	Verapamil (n=26) (%)	*p*-value
Recurrence	4 (15.4)	6 (23.1)	0.363
Complications			
Pain	24 (92.4)	23 (88.5)	0.783
Telangiectasia	5 (19.2)	0 (0)	0.025*
Dermal atrophy	7 (26.9)	0 (0)	0.005*

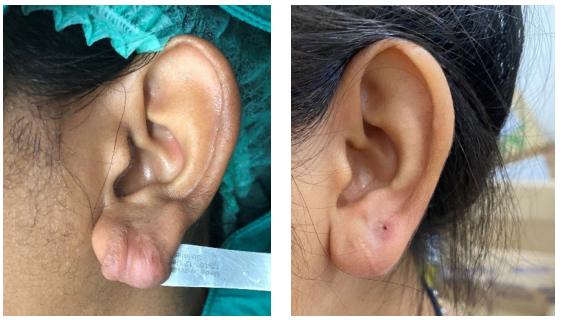
Note: Fisher Exact test

*p-values < 0.05 were defined as statistically significant



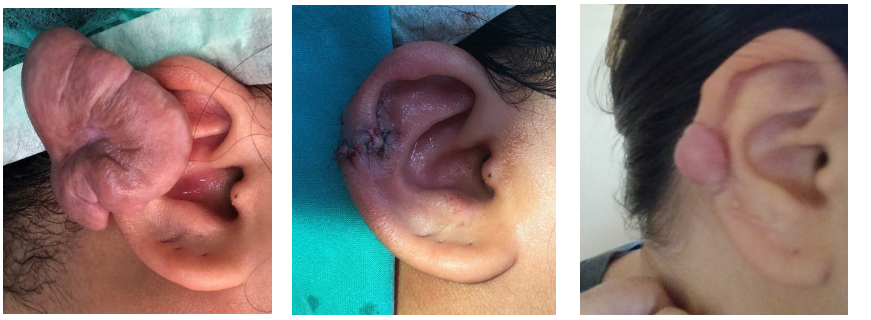
(A) (B) (C) (D)

Figure 1 The anatomic location of ear keloids; helix (A), anterior lobule (B), posterior lobule (C), and post-auricular area (D)



(A) (B)

Figure 2 A pre-operative keloid (A) and the result (B) for the one-year follow-up without recurrence



(A) (B) (C)

Figure 3 Pre-operative keloid (A), post-operative keloid (B), and recurrence (C) at 44 weeks after surgery

The VSS (Vancouver Scar Scale) assessment of post-operative scars showed significant improvement in vascularity, pliability, pigmentation, height, and total VSS scores in both group T and group V ($p<0.05$), as shown in Table 4 and Figure 4 (Line diagram).

Table 4 VSS scores compared within each group

		Mean VSS scores ± SD								
VSS score	**Drug**	**0 wks**	**4 wks**	**12 wks**	**20 wks**	**28 wks**	**36 wks**	**44 wks**	**52 wks**	***p*-value**
Vascularity	T	2.93	2.38	1.94	1.32	0.98	0.74	0.32	0.18	0.001
	V	2.87	2.64	2.32	1.87	1.21	1.08	0.94	0.40	0.001
Pliability	T	2.47	1.68	0.92	0.13	0	0	0.94	0.98	0.001
	V	2.54	2.13	1.72	1.27	0.69	0	1.87	1.93	0.001

Table 4 Continued

		Mean VSS scores ± SD								
VSS score	**Drug**	**0 wks**	**4 wks**	**12 wks**	**20 wks**	**28 wks**	**36 wks**	**44 wks**	**52 wks**	***p*-value**
Pigmentation	T	1.91	1.82	1.23	1.03	0.23	0.11	0.10	0.09	0.001
	V	1.98	1.85	1.30	1.07	0.54	0.34	0.28	0.21	0.001
Height	T	0.04	0	0	0	0	0	2.17	2.25	0.001
	V	0.15	0.04	0	0	0	0	2.25	2.00	0.001
Total VSS score	T	9.74	7.83	6.21	4.52	2.09	0.81	0.62	0.52	0.001
	V	9.15	8.09	7.74	6.18	3.24	1.74	1.44	1.32	0.001

Note: pair simple t-test

VSS score - Vancouver Scar Scale score

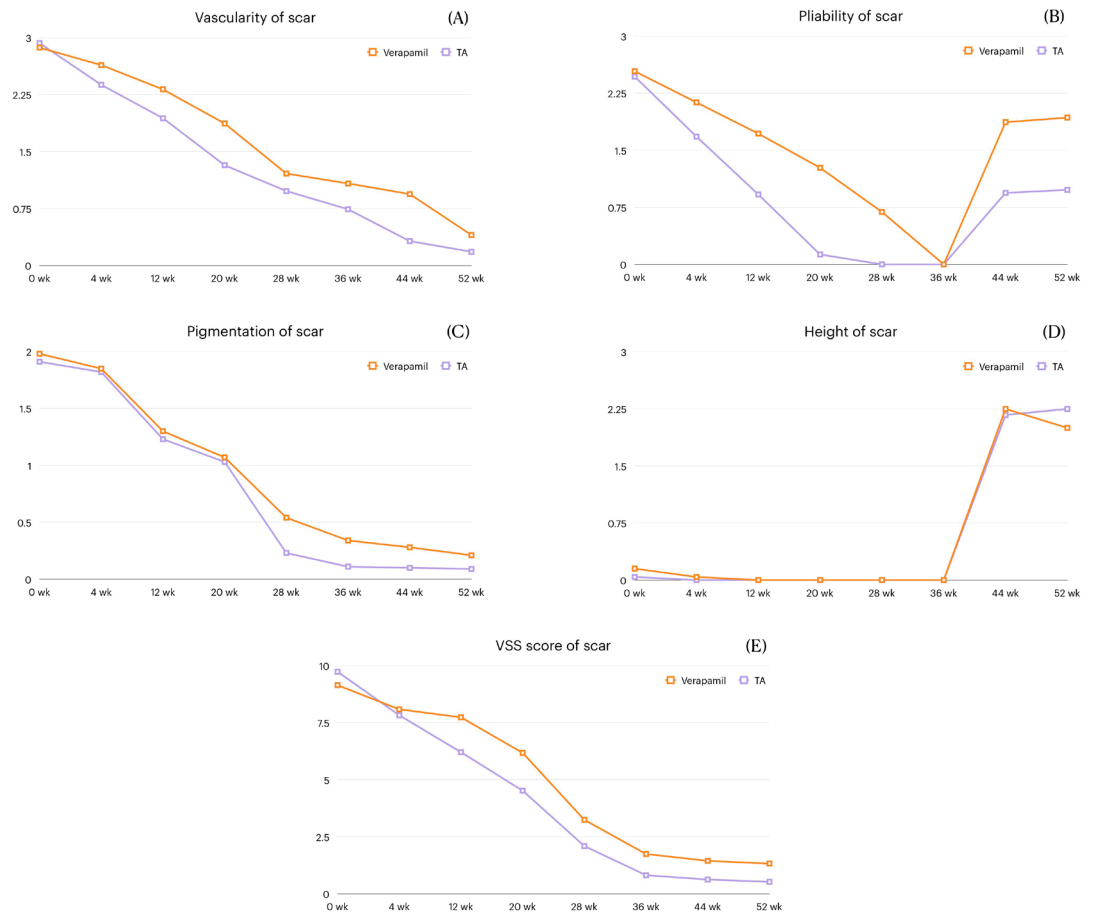


Figure 4 Line diagrams of vascularity (A), pliability (B), pigmentation (C), height (D), and VSS (E) of scars between the two treatment groups

Significant improvements in scar vascularity, pliability, and total VSS scores were found in group T, while pigmentation in group V demonstrated a faster response to treatment than in group T. The keloid height in both groups was not statistically different when measured after recurrence at the 44 week follow-up, as shown in Table 5.

Table 5 VSS scores compared between the two groups

VSS score	Mean	SD	t	*p*-value
Vascularity				
Triamcinolone	2.67	0.15	8.07	0.001
Verapamil	2.41	0.49		
Pliability				
Triamcinolone	1.43	0.43	64.33	0.001
Verapamil	0.65	0.35		
Pigmentation				
Triamcinolone	1.73	0.30	-15.31	0.001
Verapamil	1.85	0.25		
Height				
Triamcinolone	1.42	0.66	28.91	0.177
Verapamil	1.35	0.40		
Total VSS score				
Triamcinolone	9.22	0.20	50.61	0.001
Verapamil	7.75	0.08		

Note: Independent t-test
VSS score - Vancouver Scar Scale score

Discussion

Keloids are fibroproliferative disorders that result from excessive collagen deposition. They behave like benign skin tumors with continued slow growth and do not regress[1,2,4]. The mechanism of disease remains unclear. Keloids can lead to functional impairment and undesirable conditions causing cosmetic concerns, especially in highly visible areas such as the ears, face, and neck. Keloids typically occur in people 10 to 30 years old and are linked to hormonal status during puberty. Males and females are equally affected[3]. A positive family history with autosomal dominant features can cause severe keloid formation at multiple sites[3]. Our study showed a positive family history of keloids at 26.9% and 23.1% in groups T and V, respectively. The mean age of patients was 22.81±10.45 and 21.23±4.22 in groups T and V, respectively.

Females were more affected than males because the main etiology was ear piercing. Many modalities of keloid treatment include surgical excision, radiation, cryotherapy, pulsed dye laser, immunosuppressive agents (e.g., interferon alfa-2b), cultured epithelial autografts, and the use of medications such as intralesional triamcinolone or verapamil injection[4]. However, no gold standard treatment exists and successful outcomes can be achieved through a multimodality approach.

Surgical removal alone has a recurrence rate of 45 to 100%[12,13]. Kim, Dae Young et al. reported the recurrence rate for earlobe keloids after surgery as 50%[14]. Multimodality therapy combining steroid injections with surgery has shown improved response compared to monotherapies[15]. Jung JY et al. reported a 61.1% good results, with 16.6% recurrence after combined earlobe keloid excision and intralesional TA injections[16]. Intralesional steroid injections inhibited the proliferation of keratinocytes, reduced fibroblast activity, and also decreased collagen production with reduced scar height. However, corticosteroid treatment is often associated with local and systemic side effects including pain, striae, dermal atrophy, telangiectasia, dyspigmentation, and Cushing's syndrome[2,4].

Verapamil, an L-type calcium channel blocker, is commonly prescribed for treating cardiac arrhythmias and hypertension. The effectiveness of verapamil injections has been investigated by many studies since 1994[17]. Results showed that keloid resolution after perilesional surgical excision and topical silicone followed by an adjuvant treatment with intralesional verapamil hydrochloride injection was higher compared to other treatments, with 54% of cases being completely cured[18,19]. Lawrence (2004), reported a 55% cure rate for earlobe keloids treated with intralesional verapamil and pressure therapy[20]. Verapamil has also been noted for its favorable safety profile compared to TA injections. Verapamil is considered an alternative treatment for patients unable to tolerate corticosteroids[21] and is now recommended in European guidelines for intralesional keloid treatment[22].

This randomized controlled trial compared the effectiveness and safety of intralesional TA and verapamil injections in preventing keloid recurrence and improving scar appearance after surgery. Scar outcomes were evaluated using the Vancouver Scar Scale (VSS), and complications were observed. Previous studies have explored verapamil as an adjunct to surgical excision, reporting keloid recurrence rates ranging from 1.4% to 48%[14,23], and generally indicating verapamil as a safe treatment option. El-Kamel et al. found a 28.6% recurrence rate for recurrent earlobe keloids treated with keloidectomy and post-operative verapamil injections[24]. Similarly, Mane et al. reported a 28.57% recurrence rate in patients treated with keloidectomy and TA injections, compared to a lower 14.28% recurrence rate in those treated with verapamil. The average keloid recurrence-free intervals were 11.36 months for the TA group and 10.98 months for the verapamil group[25]. In our study,

the recurrence rate of ear keloids was 15.4% in group T and 23.1% in group V at 44 weeks post-surgery. The recurrence led to a worsening of the VSS score for height and pliability at week 44 of follow-up. The timing of recurrence for ear keloids can vary[24], depending on several factors such as the operative technique, the patient's skin condition, and their response to the treatment.

Two randomized studies compared intralesional verapamil with triamcinolone injections using the VSS (Vancouver Scar Scale), with results showing that verapamil reduced the height, vascularity, and pliability of keloid scars but was slower than TA[26,27]. Similarly, in our study, the VSS score assessment of post-operative scars showed significant improvement in vascularity, pliability, pigmentation, height, and total VSS score in each group ($p<0.05$) after the injections. A comparison between groups showed significant earlier improvements in scar vascularity, pliability, and total VSS score in group T, while pigmentation in group V demonstrated a faster response to treatment.

Complications induced by intralesional verapamil injections included pain after injection but no telangiectasia or dermal atrophy were detected. Intralesional verapamil injection after surgery is an option when corticosteroids cannot be used or in cases where complications from steroids are not desired.

Intralesional verapamil injections are safe, giving similar results to triamcinolone for the prevention of early keloid recurrence after surgical removal, with equal scar appearance but fewer complications.

One limitation of this study was that the follow-up period was too short. Ear keloids generally show lower recurrence rates and longer recurrence-free intervals compared to keloids at other sites[28], Follow-up periods of more than two years are suggested for more accurate results[29].

Supplementary material

Table S1 VSS scores compared between the two groups

VSS score	Drug	0-4 wks	*p*-value	0-12 wks	*p*-value	0-20 wks	*p*-value	0-28 wks	*p*-value	0-36 wks	*p*-value	0-44 wks	*p*-value	0-52 wks	*p*-value
Vascularity	T	0.55±0.58	0.001	1.02±0.88	0.001	1.58±0.22	0.001	1.95±0.36	0.001	2.17±0.34	0.001	2.57±0.34	0.001	2.67±0.15	0.001
	V	0.19±0.02		0.52±0.01		0.99±0.33		1.63±0.10		1.76±0.10		1.91±0.08		2.41±0.49	
Pliability	T	0.76±0.39	0.001	1.58±0.23	0.001	2.29±0.14	0.001	2.43±0.44	0.001	2.43±0.34	0.001	1.52±0.21	0.001	1.43±0.43	0.001
	V	0.49±0.10		0.82±0.21		1.26±0.09		1.85±0.15		2.53±0.07		0.69±0.17		0.65±0.35	
Pigmentation	T	0.09±0.02	0.001	0.67±0.01	0.548	0.86±0.24	0.001	1.67±0.09	0.002	1.78±0.05	0.001	1.80±0.02	0.001	1.73±0.30	0.001
	V	0.12±0.15		0.65±0.10		1.27±0.10		1.82±0.16		1.86±0.23		1.68±0.14		1.85±0.25	
Height	T	0.04±0.08	0.001	0	0.002	0	-	0	-	0	-	-2.13±0.94	0.296	-2.21±0.66	0.177
	V	0.09±0.05		0.10±0.07		0	-	0	-	0	-	-2.11±0.28		-1.85±0.40	
Total VSS	T	1.93±0.34	0.001	3.51±0.19	0.001	5.21±0.10	0.001	7.64±0.09	0.001	8.91±0.32	0.001	9.11±0.09	0.001	9.22±0.20	0.001
score	V	1.06±0.12		1.42±0.26		2.98±0.23		5.91±0.13		7.38±0.18		7.71±0.16		7.75±0.08	

Note: independent t-test

VSS score -Vancouver Scar Scale score

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