IJD ORIGINAL ARTICLE

Efficacy of topical silicone 5% hydrogel vs. topical hydrocortisone 1% ointment in keloid treatment measured using POSAS score: a randomized, double-blind study

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Background and Aim: Silicone-based products are often used to improve signs and symptoms of hypertrophic and keloid scars. An improved silicone product, ScarLess™ Hydrogel (SH), is a 5% silicone-based super-oxidized hydrogel meant to reduce keloid scars' vascularity, elasticity, and height. This study aimed to compare the efficacy between SH and hydrocortisone (HCT) 1% ointment in keloid treatment.

Methods: This study was a prospective, single-centered, randomized, double-blind study involving twenty-eight subjects with keloid scars. The scars were assigned randomly as Scar A and Scar B in a 1:1 ratio to receive HCT or SH under occlusion, respectively, for over 12 weeks. The Patient and Observer Scar Assessment Scale (POSAS) was used for clinical evaluation.

Results: According to the POSAS, there were significant improvements in both patient and observer scorings in both treatment arms.

Conclusion: SH has equal therapeutic efficacy as HCT in keloid treatment. SH did not present with any safety issues or side effects.

Keywords: keloid, silicone gel, scar, hypertrophic scar, POSAS

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INTRODUCTION

The wound healing process involves the inflammatory, tissue formation, and tissue remodeling phases, whereby any impairment in this mechanism will result in excessive scarring [1]. A keloid is the excessive deposition of scar tissue that extends beyond the margin of the wound of origin. It usually appears about three months after a dermal injury and can progressively enlarge up to a year after the dermal injury [2]. Histologically, the scar tissue typically demonstrates an overabundance of dermal collagen [3] composed of disorganized bundles of types I and III collagen. The overproduction of multiple fibroblast proteins, including fibronectin, is also observed, suggesting that there could be persistent wound healing signals due to a pathological cause

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or a failure in the appropriate downregulation of wound-healing cells [4].

Intralesional triamcinolone acetonide (TAC) has been widely used as the first-line treatment for keloid scars due to its significant therapeutic effects [3,5,6]. However, TAC is known to cause discomfort and pain despite its good efficacy, reducing patients' compliance. Other options for keloid treatment include liquid nitrogen cryotherapy, compression dressing, topicals such as silicone materials, corticosteroids, immunosuppressive creams and retinoids [6,7], intralesional medications [8], lasers, and surgical excision [6,7], either monotherapy or in combination with TAC.

A more convenient and effective solution that causes less pain and discomfort to patients is needed. Clinical evidence indicates that silicone-based products such as topical silicone, silicone gel sheets, and silicone cream can prevent excessive scarring and improve the outcome of already established scars [9-12]. Silicone has been shown to promote wound or scar reepithelialization, reduce transepidermal water loss, and deactivate keratinocyte signaling. An improved hydration balance in the stratum corneum aids in stabilizing the keratinocytes cascade [13].

The use of potent topical steroids under occlusion in keloid treatment has been shown to have similar efficacy to TAC injection [14]. However, they may cause local adverse effects such as erythema, hypopigmentation, and pruritis [14]. Therefore, this study opted for low potency topical corticosteroids to reduce local adverse effects. Both ScarLess™ Hydrogel (SH) and hydrocortisone (HCT) 1% ointment were applied under occlusion with waterproof and transparent film dressing, and treatment efficacy was measured. The study aimed to discover comparable or better options than topical corticosteroids in treating keloids.

METHODS

Participants and Study Design

This study was approved by the Universiti Teknologi MARA (UiTM) Research Ethics Committee (reference no. REC/344/18). Subjects were enrolled from the 1st of January 2019 to the 31st of December 2019. It was a prospective, single-centered, randomized, double-blind study conducted over 12 weeks at the Dermatology Clinic in Universiti Teknologi MARA. The primary objective of this study was to assess the efficacy of using SH, a silicone-based 5% super-oxidized hydrogel, to treat keloids in comparison to applying HCT 1% ointment, both under occlusion.

To avoid selection bias, the study subjects were selected using computer-generated simple random sampling based on the inclusion and exclusion criteria. Patients were excluded if they had prior allergic or hypersensitivity responses to any component of the medications or dressings used in the study, had active primary or secondary dermatoses superimposed on the keloid, had active skin infections, connective tissue disorders, or diabetes mellitus. Additional exclusion criteria included pregnant or lactating patients, patients who were educationally incompetent and unable to understand the Patient and Observer Scar Assessment Scale (POSAS), and those who had a history of keloid treatment in the preceding eight weeks.

There was a total of thirty-one subjects who met the inclusion criteria of being eighteen years old and above and having at least two keloid scars on the same anatomical site or having one large keloid scar exceeding 5 cm (large scar was divided into two parts for two different treatment arms) for more than six months but less than five years. There were 28 subjects who completed the study, resulting in a total of 56 scars analyzed. The scars of each subject were assigned randomly as either Scar A or Scar B in a 1:1 ratio using block randomization technique (28 scars each) to receive HCT or SH under occlusion, respectively. The subjects were advised to apply the treatment at the allocated scar as instructed by the research nurse.

Written informed consent and written questionnaires filled with personal details and clinical information were collected at the start of the study. The subjects were followed with a standardized protocol (Figure 1).

Materials

The 1% HCT ointment was manufactured by Hoe Pharmaceuticals Sdn. Bhd., Malaysia. Its inactive ingredients consist of liquid paraffin and white soft paraffin. The SH, which consists of 5% silicone, was manufactured by Oculus Technologies of Mexico based on the Microcyn® Technology, which involves highly stable small molecule oxychlorine compounds. Both topicals were applied on the respective scars

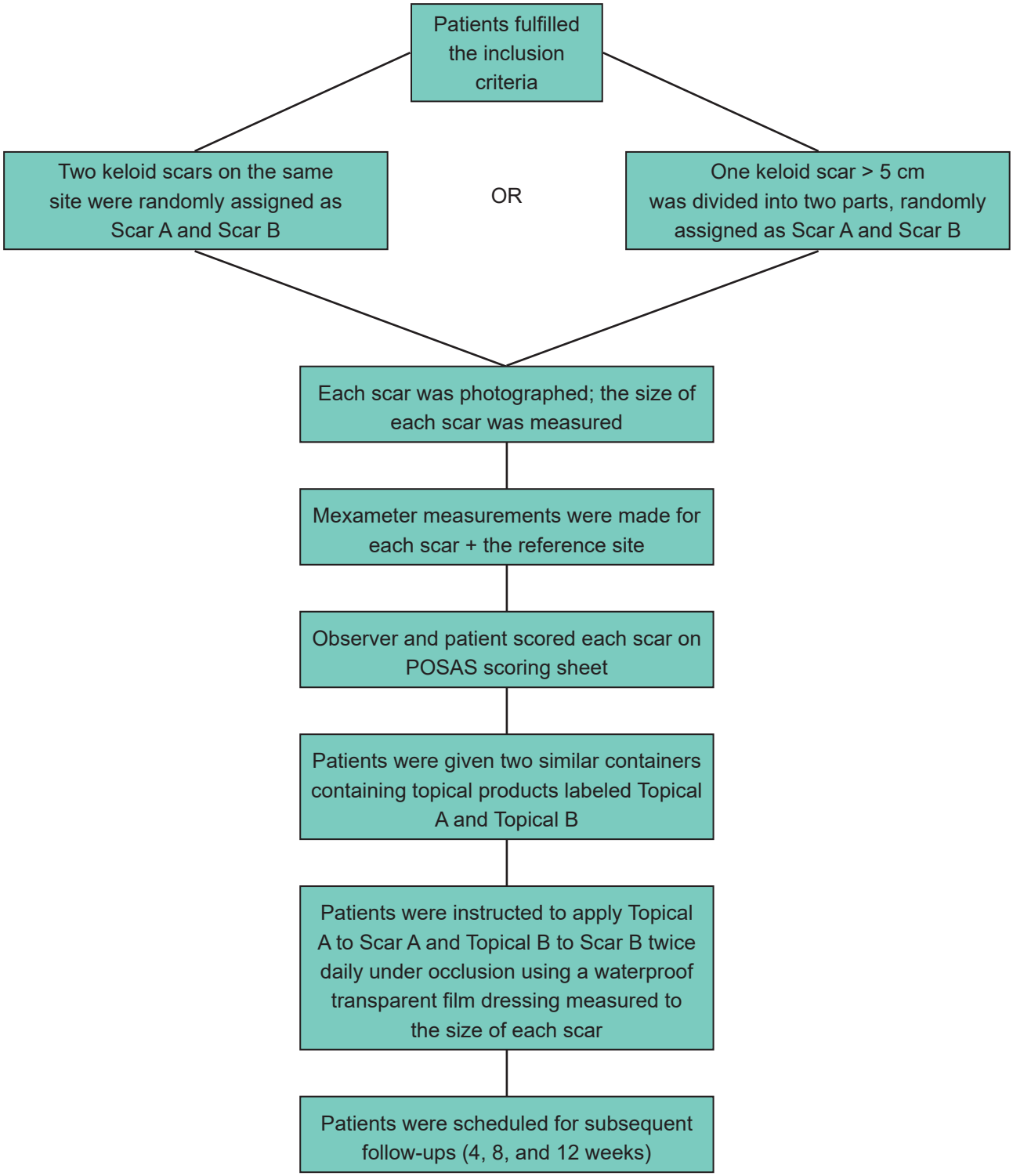

Figure 1. Study protocol

under occlusion using a waterproof transparent film dressing twice daily, with an approximate twelve-hour interval in between.

The clinical trial code is IRCT20220727055565N1.

Data Collection and Outcome Measures

Scoring of Patient and Observer Scar Assessment Scale (POSAS)

The POSAS is a validated scoring tool that

includes the perspectives of both the patient and the observer/investigator [15-17]. The assessment allows the subject and observer to measure two different sets of six parameters. Parameters including pain, itchiness, color, stiffness, thickness, and irregularity of the keloid are evaluated by the subjects with the patient assessment scale. On the other hand, the vascularity, pigmentation, thickness, pliability, relief, and surface area of the keloids are assessed by the observer with the observer assessment scale. In our study, an investigator evaluated the scars from week 0 (baseline) to week 12 across four-week intervals. The patient POSAS was also scored by the subjects in the same way from week 0 to week 12.

Statistical Analysis

The data were analyzed with Statistical Package for Social Science (SPSS) software version 26. Descriptive statistics were performed to analyze the demographic data encompassing age, gender, and ethnicity, as well as the cause, duration, history of previous treatment, and site of the keloids. The Shapiro-Wilk test was performed to test the normality of the data. Per-protocol was applied in the analysis. The mixed-method within-between subjects repeated measure analysis of variance (ANOVA) was used to compare the mean POSAS scores between both treatment arms at weeks 0, 4, 8, and 12. P-values of < 0.05 were considered statistically significant. Sphericity was assessed using Mauchly's test of sphericity. The data were analyzed using the sphericity assumption if the test was significant. On the other hand, if the test was not significant, the Huynh-Feldt correction was used if the P-value was higher than 0.70, or the Greenhouse-Geisser correction was used if the P-value was lower than 0.70 to adjust the degree of freedom.

RESULTS

Out of the total thirty-one subjects who enrolled in this study, two subjects withdrew voluntarily. One withdrew due to discomfort upon applying the 1% HCT ointment. The other was lost to follow-up, giving a response rate of 90.3%.

The descriptive statistics of the subjects are displayed in Table 1. In this study cohort, most of the subjects were female (64.3%), Malay (96.4%), and had an income between RM 1,000 to RM 5,000 (53.6%). Only 10.7% of the subjects had a history of allergy.

Table 1. Descriptive statistics of the demographic data and clinical characteristics of the study cohort (N = 28)

Age, years	(N = 28), n (%)	Mean ± SD
Gender		31.82 ± 9.39
Female	18 (64.3)	
Male	10 (35.7)	
Ethnicity		
Malay	27 (96.4)	
Chinese	1 (3.6)	
Income		
Less RM 1000	6 (21.4)	
RM 1000-RM 5000	15 (53.6)	
More than RM 5000	7 (25.0)	
History of Allergy		
Yes	3 (10.7)	
No	25 (89.3)	
Duration of keloids		
Less than 1 year	2 (7.1)	
1 - 3 years	21 (75.0)	
3 - 5 years	5 (17.9)	
Cause of Keloid		
Acne	13 (46.4)	
Surgery	6 (21.4)	
Varicella Zoster	1 (3.6)	
Trauma	1 (3.6)	
Vaccination	1 (3.6)	
Others	6 (21.4)	
Previous treatment		
None	19 (67.9)	
Moisturizer	2 (7.1)	
Intralesional steroid	4 (14.3)	
Surgery	2 (7.1)	
Others	1 (3.6)	
Location of Scar A		
Shoulder	8 (31.3)	
Trunk	8 (31.3)	
Upper limb	5 (15.6)	
Lower abdomen	4 (12.5)	
Others	3 (10.7)	
Location of Scar B		
Shoulder	8 (28.6)	
Trunk	8 (28.6)	
Upper limb	5 (17.9)	
Lower abdomen	4 (14.3)	
Others	3 (10.7)	

RM: Ringgit Malaysia

The characteristics of the keloid scars are shown in Table 1. It was found that 75% of the subjects had keloid scars for one to three years. Besides, the data showed that acne was the predominant cause of keloid scars among the subjects, accounting for

46.4% of the etiology. The keloid scars were mostly found on the subjects' shoulders (31.3%) and trunk (31.3%). Approximately 67.9% of the subjects were treatment-naïve.

POSAS Scoring

Table 2 shows the patient and observer scores on the POSAS on Scar A and Scar B at weeks 0 (baseline), 4, 8, and 12. Figure 2a shows the trends of the patient scores of POSAS on Scar A and Scar B, which constantly declined from baseline to week 12. Figure 2b shows the trends of the observer scores of POSAS on Scar A and Scar B, which had a similar pattern as that of the patient scores of POSAS.

The within-subjects analysis (refer to Table 3) showed that there were significant differences over

Table 2. The patient and observer scores of the POSAS at weeks 0 (baseline), 4, 8, and 12 for Scar A (HCT) and Scar B (SH)

POSAS Total	Week	Scar A (HCT)	Scar B (SH)
Patient scores of POSAS	Week 0	40.25 ± 9.59	40.13 ± 9.74
	Week 4	32.88 ± 9.30	33.84 ± 9.06
	Week 8	29.03 ± 9.71	29.19 ± 9.10
	Week 12	24.53 ± 9.67	25.59 ± 9.04
Observer scores of POSAS	Week 0	38.63 ± 9.77	39.59 ± 10.51
	Week 4	34.69 ± 10.73	35.531 ± 11.36
	Week 8	29.09 ± 7.54	28.94 ± 9.46
	Week 12	21.84 ± 7.79	23.09 ± 7.49

SH, ScarLess™ Hydrogel; HCT, hydrocortisone

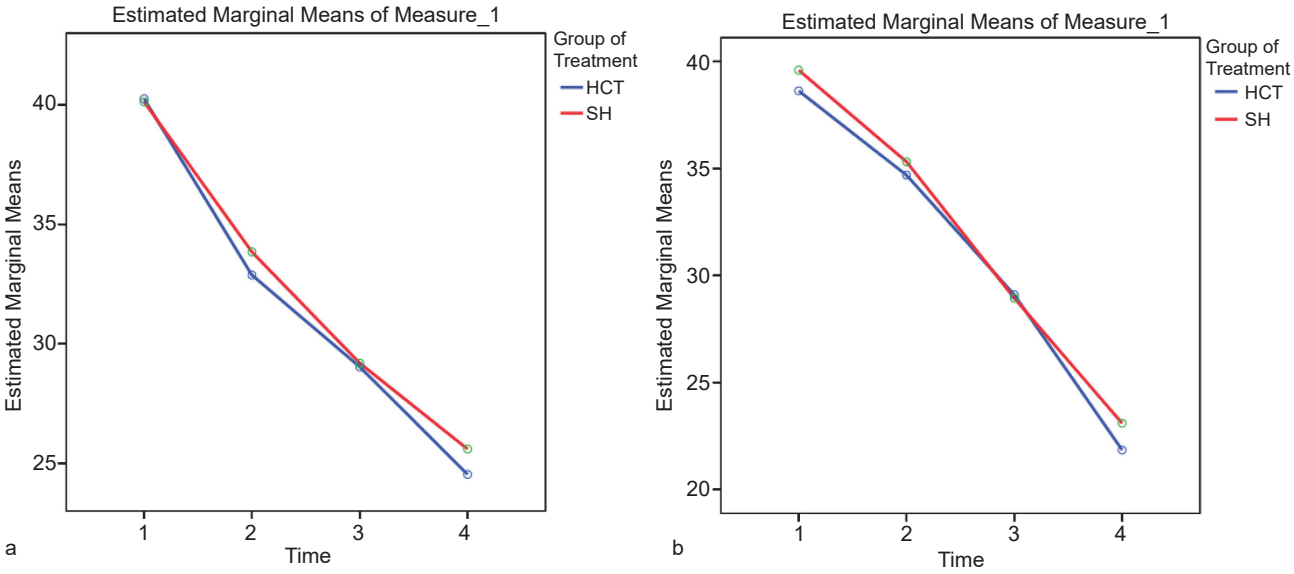

Figure 2. (a) Comparison between the mean patient scores of POSAS on Scar A (HCT) and Scar B (SH) at four time points, namely weeks 0 (baseline), 4, 8, and 12. (b) Comparison between the mean observer scores of POSAS on Scar A (HCT) and Scar B (SH) at four time points, namely weeks 0 (baseline), 4, 8, and 12.

Table 3. Within-subjects and between-subjects analyses on the effectiveness of ScarLess™ Hydrogel and hydrocortisone on the keloids based on the patient and observer scores of the POSAS

POSAS Total	Analysis	F (df)	*P*-value	Partial eta
Patient scores of POSAS	Within-subjects	80.789** (2.206, 306.753)	< 0.001*	0.566
	Between-subjects	0.067 (1, 62)	0.797	0.001
Observer scores of POSAS	Within-subjects	141.368*** (1.710, 106.007)	< 0.001*	0.695
	Between-subjects	0.105 (1, 62)	0.747	0.002

* Statistically significant at $\alpha = 0.05$ (Repeated measures ANOVA analysis)
** Huynh-Feldt degree of freedom adjustment
*** Greenhouse–Geisser degree of freedom adjustment

Table 4. Pairwise comparison between times for the patients and observer scores of the POSAS stratified by Scar A and Scar B

	Time 1	Time 2	Scar A		Scar B	
			Mean difference (95% Confidence Interval)	*P*-value	Mean difference (95% Confidence Interval)	*P*-value
Patient scores of POSAS	Week 0	Week 4	7.38 (2.47, 11.28)	< 0.001	6.28 (2.69, 9.87)	< 0.001
	Week 0	Week 8	11.22 (6.09, 16.35)	< 0.001	10.98 (6.58, 15.30)	< 0.001
	Week 0	Week 12	15.72 (10.39, 21.05)	< 0.001	14.53 (10.01, 19.06)	< 0.001
	Week 4	Week 8	3.84 (-0.01, 7.70)	0.051	4.56 (1.19, 8.13)	0.004
	Week 4	Week 12	8.34 (4.17, 12.52)	< 0.001	8.25 (3.96, 12.54)	< 0.001
	Week 8	Week 12	4.50 (1.96, 7.04)	< 0.001	3.95 (1.20, 5.98)	0.001
Observer scores of POSAS	Week 0	Week 4	3.94 (1.92, 5.96)	< 0.001	3.28 (2.24, 6.33)	< 0.001
	Week 0	Week 8	9.53 (6.43, 12.64)	< 0.001	10.66 (7.67, 13.64)	< 0.001
	Week 0	Week 12	16.78 (11.87, 21.70)	< 0.001	16.50 (12.79, 20.22)	< 0.001
	Week 4	Week 8	5.59 (2.55, 8.64)	< 0.001	6.37 (3.62, 9.14)	< 0.001
	Week 4	Week 12	12.84 (7.68, 18.01)	< 0.001	12.22 (8.22, 16.21)	< 0.001
	Week 8	Week 12	725 (3.98, 10.52)	< 0.001	5.84 (3.22, 8.47)	< 0.001

time in both the patient and observer scores of the POSAS from across the four-week intervals from week 0 to week 12, with large effect sizes (partial eta > 0.15). The pairwise comparison (refer to Table 4) also showed that both the patient and observer scores decreased significantly ($P < 0.05$) over time, except for the change in patient scores on Scar A from week 4 to week 8.

The between-subjects analysis showed no significant differences between the treatment arms in both the patient and observer scores. Therefore, it can be concluded that there is no difference in the effectiveness of HCT and SH in treating keloid scars.

Treatment safety

One subject defaulted due to having reported a burning and itching sensation upon applying the 1% HCT ointment, whereas there were no reported side effects of SH. Mild itchiness and rash were observed on the surrounding edges of the transparent film dressing in four subjects, and these symptoms were resolved after the size of the dressing was adjusted.

DISCUSSION

Similar to previous studies, females comprised the majority of the subjects involved in this study, with a subject ratio of 2:1 [18,19]. This can be attributed to a more profound concern regarding physical aesthetics among females. The mean age of the subjects was 31.82 ± 9.39 years, with the youngest being 18 and the oldest being 63 years old. This was consistent with the findings of other studies reporting that keloid patients' mean age fell within the range of 10 to 30 years of age [20-22].

The majority of the subjects were of Malay ethnicity, which correlates with the overall clinic attendees, where 70% are Malay patients. Moreover, similar demographics reflecting Malays as the majority group were also reported in another two studies on keloids conducted in Malaysia in the recent five years [14,23]. In contrast, a study conducted at Kuala Lumpur General Hospital reported a high incidence of keloids in Chinese patients (47%) [24]. Ethnicity is one factor that affects keloid formation, with a higher prominence in colored individuals [24-26] due to certain genetic properties [27,28]. Generally, Malays have either Fitzpatrick skin type I, II, III, IV, V, or VI skin, with 53% having type III skin [29]. On the other hand, Malaysian Chinese have either Fitzpatrick skin type I, II, III or IV, with 64% having skin type II. This may explain the higher keloid incidence in Malays compared to Chinese, as Malays generally have a darker skin tone. However, further data are required to support this hypothesis of the higher likelihood of keloid development in colored skin, such as the data of keloid incidence among Malaysian Indians who typically have Fitzpatrick skin type IV, V or VI.

The majority of the keloids of the study cohort were formed on the shoulder (28.6%), which is similar to the findings of another local study [9]. Besides, acne was also the most prominent etiology in both studies. Nevertheless, two large studies in Asia reported differently, in which one of the studies reported the chest as the most frequent site of keloids [20], and

the other, which was carried out over eight years, reported that as high as 34% of the keloids (336 out of 1,000) occurred on the presternal region [30].

In treating keloids, corticosteroids act as anti-inflammatory agents and disrupt collagen and glycosaminoglycan synthesis by breaking down excessive collagen and fibroblasts [31]. A study showed that topical steroids used under occlusion dressing are comparable to TAC injection in treatment efficacy [14]. Hence, occlusion dressing was used in this study to increase the absorption of the topical corticosteroid. There were other relevant studies that supported the efficacy of topical corticosteroids in scar treatment, except that they were not specifically targeting established keloid scars [32,33]. Furthermore, topical HCT ointment was reported to have successfully eradicated hypertrophic post-cesarean scars after three months of application [32]. Improvements in keloids were observed in the study cohort of this study after a similar duration of treatment.

One subject treated with HCT reported an itching and burning sensation and withdrew from this study. This was consistent with the findings of a previous study on the adverse effects of topical steroids in the long term [34]. No obvious hypopigmentation was observed in this study after three months of HCT ointment application. However, reduced erythema was observed.

A significant improvement in keloids comparable to the HCT treatment arm was observed in the SH treatment arm throughout the 12 weeks. This finding was congruent with the randomized controlled trial by Meseci *et al.*, which concluded that there was no difference between methylprednisolone cream and silicone gel in terms of their treatment efficacy on post-cesarean scars [32].

Silicone products in the gel form have shown an advantage over silicone sheets due to their easy administration and suitability, even for sensitive skin [35]. Besides, another advantage of silicone gel is its self-drying property [36]. With regards to that, none of the subjects in this study showed any evidence of allergy or irritation towards SH. The silicone content of SH at 5% may have eliminated allergic reactions, but may also reduce the efficacy.

A recent systemic review that compared the effectiveness of silicone gel and silicone gel sheets in scar treatment showed that the keloid improvement was significant for both [37]. Moreover, there were studies that reported sufficient evidence of scar management with silicone product vs. placebo. Some comparative studies indicate that silicone materials are better than TAC [38,39].

Limitations

This study only lasted for 12 weeks, whereas according to a review article, many studies have shown that a duration of six months or longer is needed to observe continuous positive outcomes of silicone material in treating keloids [12]. Nevertheless, a more prolonged study duration was not considered in this study because significant improvements of the scars were observed within the 12 weeks study period. Furthermore, the subjects' compliance with the daily application of the treatments and occlusive dressing throughout the study period could represent a confounding factor. The subjects' compliance is expected to be lower when the study period is longer, hence another reason why a longer study period was not applied.

CONCLUSION

In this study, the therapeutic efficacies of HCT and SH on keloid scars were found to be equal. Unlike topical steroids, the long-term safety of silicone gel has been proven [40], along with its painless and convenient properties, making it a good alternative treatment for keloid scars.

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Authors' contributions

Liyana D Aminuddin (L.D.A) and Tarita Taib (T.T) were involved in conceptualization of the paper. L.D.A and Sabrina A Wahab (S.A.W) performed the data collection. L.D.A, Mohan Arumugam (M.A) and Mohamad Rodi Isa (M.R.I) performed data analysis and interpretation. L.D.A drafted the original manuscript. S.A.W, T.T, M.R.I and M.A reviewed and critiques the drafted manuscript. L.D. and T.T performed the manuscript editing. All authors have

critically reviewed and approved the final draft.

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Disclosure

Results and analysis of research are derived and discussed independently from the sponsor company

Conflict of interest: None declared.

REFERENCES

1. Eming SA, Martin P, Tomic-Canic M. Wound repair and regeneration: mechanisms, signaling, and translation. Sci Transl Med. 2014;6(265):265sr6.
2. Brissett AE, Sherris DA. Scar contractures, hypertrophic scars, and keloids. Facial plast Surg. 2001;17(04):263-72.
3. Gauglitz GG, Korting HC, Pavicic T, et al. Hypertrophic scarring and keloids: pathomechanisms and current and emerging treatment strategies. Mol Med. 2011;17(1):113-25.
4. Sephel G, Sephel GC, Davidson JM. Repair, regeneration and fibrosis in: rubin's pathology: clinicopathologic foundations of medicine. 7th Edition. Strayer DS, Rubin E. Wolters Kluwer. 2015.
5. Mustoe TA, Cooter RD, Gold MH, et al. International clinical recommendations on scar management. Plast Reconstr Surg. 2002;110(2):560-71.
6. Nast A, Eming S, Fluhr J, et al. German S2k guidelines for the therapy of pathological scars (hypertrophic scars and keloids). J Dtsch Dermatol Ges. 2012;10(10):747-62.
7. Chike-Obi CJ, Cole PD, Brissett AE. Keloids: pathogenesis, clinical features, and management. Semin Plast Surg. 2009;23(03):178-84.
8. Mustoe TA, Cooter RD, Gold MH, et al. International clinical recommendations on scar management. Plast Reconstr Surg. 2002;110(2):560-71.
9. Kim S, Choi TH, Liu W, et al. Update on scar management: guidelines for treating asian patients. Plast Reconstr Surg. 2013;132(6).
10. Meaume S, Le Pillouer-Prost A, Richert B, et al. Management of scars: updated practical guidelines and use of silicones. Eur J Dermatol. 2014;24(4):435-43.
11. Monstrey S, Middelkoop E, Vranckx JJ, et al. Updated scar management practical guidelines: non-invasive and invasive measures. J Plast Reconstr Aesthet Surg. 2014;67(8):1017-25.
12. Mustoe TA. Evolution of silicone therapy and mechanism of action in scar management. Aesth Plast Surg. 2007;32(1):82.
13. Suetake T, Sasai S, Zhen Y-X, et al. Effects of silicone gel sheet on the stratum corneum hydration. Br J Plast Surg. 2000;53(6):503-7.
14. Nor NM, Ismail R, Jamil A, et al. A randomized, single-blind trial of clobetasol propionate 0.05% cream under silicone dressing occlusion versus intra-lesional triamcinolone for treatment of keloid. Clin Drug Investig. 2017;37(3):295-301.
15. Draaijers LJ, Tempelman FRH, Botman YAM, et al. The patient and observer scar assessment scale: a reliable and feasible tool for scar evaluation. Plast Reconstr Surg. 2004;113(7).
16. Verhaegen PDHM, van der Wal MBA, Middelkoop E, et al. Objective scar assessment tools: a clinimetric appraisal. Plast Reconstr Surg. 2011;127(4).
17. van der Wal MBA, Tuinebreijer WE, Bloemen MCT, et al. Rasch analysis of the patient and observer scar assessment scale (POSAS) in burn scars. Qual Life Res. 2012;21(1):13-23.
18. Lee CP. Keloids—their epidemiology and treatment. Int J Dermatol. 1982;21(9):504-5.
19. Sun L-M, Wang K-H, Lee Y-CG. Keloid incidence in asian people and its comorbidity with other fibrosis-related diseases: a nationwide population-based study. Arch Dermatol Res. 2014;306(9):803-8.
20. Lu W-s, Zheng X-d, Yao X-h, et al. Clinical and epidemiological analysis of keloids in Chinese patients. Arch Dermatol Res. 2015;307(2):109-14.
21. Adegbidi H, Atadokpede F, Do Ango-Padonou F, et al. Keloid acne of the neck: epidemiological studies over 10 years. Int J Dermatol. 2005;44(s1):49-50.
22. Allah KC, Yéo S, Kossoko H, et al. Keloid scars on black skin: myth or reality. Ann Chir Plast Esthet. 2013;58(2):115-22.
23. Tee SH, Ng TG, Azizan NZ. Comparison of the efficacy of intralesional triamcinolone acetonide and silicone gel sheeting for the treatment of keloids. Notice to Authors. 2018:10.
24. Bock O, Schmid-Ott G, Malewski P, et al. Quality of life of patients with keloid and hypertrophic scarring. Arch Dermatol Res. 2006;297(10):433.
25. Al-Attar A, Mess S, Thomassen JM, et al. Keloid pathogenesis and treatment. Plast Reconstr Surg. 2006;117(1):286-300.
26. Berman B, Bieley HC. Keloids. J Am Acad Dermatol. 1995;33(1):117-23.
27. Brown J, Bayat A. Genetic susceptibility to raised dermal scarring. Br J Dermatol. 2009;161(1):8-18.
28. Shih B, Bayat A. Genetics of keloid scarring. Arch Dermatol Res. 2010;302(5):319-39.
29. Md Z, Shamsuddin K, Bukhary N, et al. The reliability of fitzpatrick skin type chart comparing to mexameter (mx 18) in measuring skin color among first trimester pregnant mothers in petaling district, malaysia. Malaysian J Pub Health Med. 2016;16:59-65.
30. Ramakrishnan KM, Thomas KP, Sundararajan CR. Study of 1,000 patients with keloids in South India. Plast Reconstr Surg. 1974;53(3):276-80.
31. Boyadjiev C, Popchristova E, Mazgalova J. Histomorphologic changes in keloids treated with Kenacort. J Trauma. 1995;38(2):299-302.

32. Meseci E, Kayatas S, Api M, et al. Comparison of the effectiveness of topical silicone gel and corticosteroid cream on the pfannenstiel scar prevention - a randomized controlled trial. Ginekol Pol. 2017;88(11):591-8.
33. Meseci E. Assessment of topical corticosteroid ointment on postcesarean scars prevention: a prospective clinical trial. Pak J Med Sci. 2019;35(2):309-14.
34. Coondoo A, Phiske M, Verma S, et al. Side-effects of topical steroids: a long overdue revisit. Indian Dermatol Online J. 2014;5(4):416-25.
35. Puri N, Talwar A. The efficacy of silicone gel for the treatment of hypertrophic scars and keloids. J Cutan Aesthet Surg. 2009;2(2):104-6.
36. Hsu KC, Luan CW, Tsai YW. Review of silicone gel sheeting and silicone gel for the prevention of hypertrophic scars and keloids. Wounds. 2017;29(5):154-8.
37. Hsu K-C, Luan CW, Tsai Y-W. Review of silicone gel sheeting and silicone gel for the prevention of hypertrophic scars and keloids. Wounds. 2017;29.
38. Sproat JE, Dalcin A, Weitauer N, et al. Hypertrophic sternal scars: silicone gel sheet versus kenalog injection treatment. Plast Reconstr Surg. 1992;90(6):988-92.
39. Kelemen O, Kollár L, Menyhei G. A comparative clinical study of the treatment of hypertrophic scars with either intralaesional steroid or silicone gel sheeting. Magy Seb. 2007;60(6):297-300.
40. Medhi B, Sewal RK, Kaman L, et al. Efficacy and safety of an advanced formula silicone gel for prevention of post-operative scars. Dermatol Ther (Heidelb). 2013;3(2):157-67.