Original Article

Effectiveness, Safety, and Satisfaction of Silicone Pro Gel in Prophylaxis and Management of Post-Operative Scar: A Randomized, Double-Blinded, Placebo-Controlled Study

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Objective: To assess the effectiveness and side effects of Silicone Pro Gel to alleviate scar development among the pregnant women with the first cesarean section, and their satisfaction.

Materials and Methods: The present study was a randomized, double-blinded, placebo-controlled study among the women with transverse abdominal wound of the first cesarean section. The formation and improvement of scar was assessed by intervention-blinded investigators and patients in terms of redness, height, surface regularity, and attribute of the scar. Ninety women were enrolled into either the study drug or placebo groups by computerized randomization (C0). Women in both groups applied the allocated drugs within 7 to 10 days after cesarean section and had to apply the allocated drugs twice a day. The re-assessment was done at 28±4 days (C1), at 56±4 days (C2) and at 84±4 days (C3).

Results: About 76% of women completed the study. The present study product performed better than the placebo in terms of formation of the wound, including height, surface regularity, and attribute of the scar. Neither side effects nor serious complications caused by the study drug were reported. Most women reported high satisfaction and there was no difference of participants' perception toward the wound between groups.

Conclusion: Silicone Pro Gel performed better in terms of alleviation of scar development post cesarean section with high participants' satisfaction.

Keywords: Scar, Photograph assessment, Investigator, Participant

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Wound scars after surgery are a natural part of the healing process and body mechanism of dermal disruption caused by a variety of skin injury ranging from hypertrophic scars, keloid scars, and atrophic scar. Hypertrophic scars and keloids show differences in morphologically and histologically. Keloid hypertrophic scar appear as an elevated scar confined within the boundaries of defect, while keloid characterize by an expanded scar with projection beyond the original wound. Histologically, keloids are composed of thick, hyalinized collagen bundles. Hypertrophic scars had fascicles of myofibroblasts with disorganized orientation. Atrophic scar is another form that also has an abnormal expression of collagen blocking regeneration. This scar type is depressed because the collagen bundles do not overextend the tissue[1,2].

Hypertrophic scar and keloid have different clinical and histopathological presentations suggesting difference in pathogenesis. Genetic, melanin in the skin, and hormone are important predisposing factors to keloids. Scar frequently determine the aesthetic impairment and may be symptomatic, causing itching, tenderness, pain, sleep disturbance, anxiety, and depression due to cosmetic concerns[3]. Other psychological sequelae include post-operation stress

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reactions, loss of self-esteem, and stigmatization leading to a diminished quality of life, in particular among women[4].

Many techniques for management of hypertrophic scars and keloids have been proven through extensive use of multi-tools, but few topical treatments have been scientifically supported by prospective studies with adequate control groups[5]. Several new therapies showed good results in small-scale trials, but these have not been repeated in larger trials with long-term follow-up and well research designed[5,6]. It is much more efficient to prevent hypertrophic and keloid scars than to treat them. Prevention implies using a therapy with the aim of reducing the risk of a problem scar evolving. Vitamin C, one of the key alleviated scar treatments, is well-known for its antioxidant activity on scar management[6]. It can improve the wound healing process and improve the scar appearance by preventing hyper proliferation of melanin synthesis. Moreover, silicone gel is a well-known product for prevention and management of skin scar. Several clinical studies showed the effectiveness of silicone on the scar appearance[1,7-9]. The major mode of action is silicone acts as a physical barrier against pathogenic intrusion and prevents trans epidermal water loss (TEWL).

Silicone Pro Gel also includes mucopolysaccharide polysulphate (MPS), which also has therapeutic effects on the tissue proliferation and wound healing to reduce scar formation. MPS is a heparinoid substance, which has anti-inflammation, fibrinolytic, and tissue regeneration properties, and improves the hydration of the skin and scar constituents by improving hyaluronan synthesis[10]. Furthermore, there has been a report that Silicone Pro Gel causes no side effects such as burning sensation among users[11]. The present study aims to determine its effectiveness on the transverse abdominal wound.

Materials and Methods

The randomized, double-blinded, placebo-control study was conducted at the Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital between March and October 2017. The ethical approval was derived from the Siriraj Institutional Review Board (COA. No.130/2017).

Study participants

All women who gave birth by cesarean section for the first time at Siriraj Hospital were approached on post-operative day 2. All participants underwent cesarean section performed by second- or third-year residents. The inclusion criteria were first-time transverse abdominal wound, gestational age (GA) at delivery of 37 weeks or more and body mass index (BMI) of less than 35 kg/m². The exclusion criteria included having any immunocompromised conditions such as human immunodeficiency virus (HIV) infection and systemic lupus erythematosus (SLE), having any evidence of peri-partal infection such as high grade fever, rupture of membranes at 24 hours prior to delivery or earlier, and having severe obstetric complications such as severe pre-eclampsia and placenta accreta.

Methods

After being approached on post-operative day 2, all eligible participants were invited to participate in the study on post-operative day 7 to 10, which was the time of the authors' routine wound evaluation. Following the explanation about the study, the participants signed inform consent. In the initial visit (C0), they were asked about demographic data, received wound assessment by investigator, and the wound was photographed. Computer-generated randomization was done using block-of-four. The allocation of the participants into the 'study drug' or 'placebo gel' group was done in sealed envelope, which was blinded to both the participants and the investigators. Instruction for the application of the gel was given to each participant. Then, women were asked to return to the study site at 28±4 days (C1), at 56±4 days (C2), and at 84±4 days (C3). On each visit, the used tubes of the gel were checked for the compliance, and the abdominal wound was examined by the same investigator (Leeyaphan C) and photographed. The participants' perception as well as satisfaction was assessed.

Study materials

The present study drug was 'Silicone Pro Gel (Medinova, Thailand)' which is a 10 g tube containing clear and odorless gel. The placebo drug was packaged by the same company using clear non-medicated gel. The outer appearance of both study drug and placebo drug looked similar and were labeled using numerical code. Participants were instructed in detail to apply the drug or placebo to their abdominal wound scar two times a day, in the morning after bath and in the evening after bath. The wound scar should be dried up with a small towel before each study material applied. A small amount of the drug or placebo, the size of green pea, was asked to be used at each application. On average, one tube could be used for four weeks,

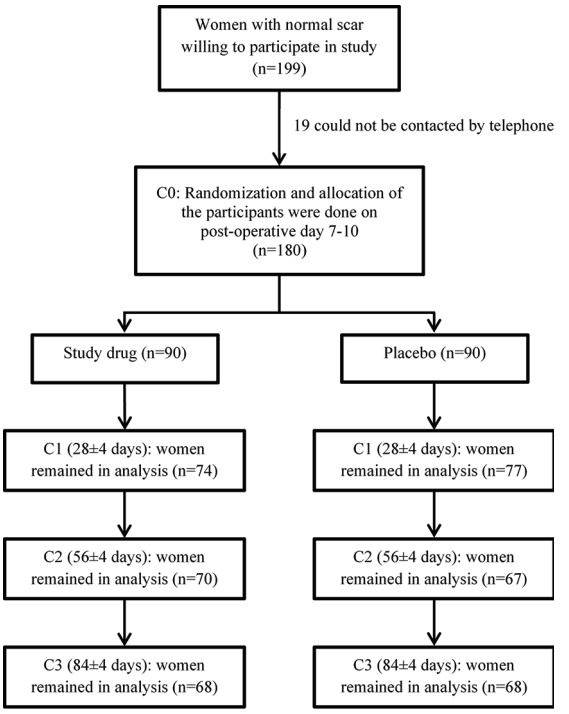

Figure 1. Patient flow chart.

therefore, each participant was prescribed one tube in between the two visits.

Outcome measures

The measurement of scar was assessed by both investigators and participants. The parameters of wound evaluation were redness (pale or pink, red, purple), surface (1=regular to 3=irregular), and attribute of the scar (smooth, medium, stiff). Participant's perception was evaluated by self-scoring (1=best and 10=worst) regarding pain, itching, color, thickness, and irregularity of skin. The evaluation took place four times respectively (C0, C1, C2, C3).

Photograph assessment was done using a 24 million pixel digital camera at 20 cm-distance from the wound without zooming or using any special techniques. The photograph was taken twice on the top view and the lateral view. Each set of photographs was coded using numbers and evaluated by a blinded obstetrician. The parameters included height (millimeter) and width (millimeter).

Sample size calculation and statistical analysis

IBM SPSS Statistics for Windows, version 20.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis. Descriptive statistics were used as appropriate, including n (%), mean ± standard deviation (SD) and median (interquartile range [IQR]). To compare categorical data, chi-square or Fisher's exact test was used. Distribution of continuous data was tested using Shapiro-Wilk test. Between groups, t-test was used to compare parametric data; and Wilcoxon rank sum test was used to compare non-parametric data. The improvement of scar in each group was tested by paired t-test for parametric data and Wilcoxon signed rank test for non-parametric data. A p-value of less than 0.05 was considered statistical significance.

Sample size calculation was based on a previous randomized trial conducted in women who underwent cesarean section. The difference of the Patient and Observer Scar Assessment Scale (POSAS) was 7[12]. The required sample size was 61 in each group when indicated alpha=0.05, two-sided test, power=97, and common SD=10.0. The estimated drop-out rate was 50%. The recruited number of participants in each group was 90.

Results

Of 199 eligible participants, 180 were included into the randomization (90 participants in each group). Sixty-eight participants were present at C3 (75.6%) (Figure 1). The collection of used gel tubes at each visit showed that more than 80% of each tube was finished.

There was no significant difference of demographic data between women using Silicone Pro gel and those using placebo. The participants were around 30-year-old. None of them were morbidly obese. More than half finished University and had office jobs. Almost all were married or co-habiting. Three quarters were first-time mothers. Cesarean section operations were performed by the second-year residents at 82.2% (85.6% versus 78.9% in 'Silicone Pro Gel' versus 'placebo' group). The operative time was around 40 minutes and the estimated blood loss was 400 mL. Hospital stay was less than five days in most cases (Table 1).

Table 2 shows that, according to investigator assessment, Silicone Pro Gel had significant superiority in terms of surface regularity and attribute of the scar ($p<0.05$ for all). The height of scar at C3 was 1.5 (0 to 2) mm versus 2 (0 to 3) mm and the width of scar at C3 was 3 (2 to 5) mm versus 3.5 (2 to 6) mm for Silicone Pro Gel versus placebo drug. Based on photograph assessment, the comparison with the prior evaluation showed higher proportion of women with thicker and wider scar in the 'placebo' group (Figure 2).

The participants' perception toward the scar formation improved from C0 to C3 in all domains and there was no significant difference between groups (Figure 3). Global satisfaction was explored among the participants and showed comparable results between women using Silicone Pro Gel and those using placebo drug in that 50.7% versus 41.2%

Table 1. Demographic data of the participants (n=180)

	Placebo (n=90) n (%)	Silicone Pro Gel (n=90) n (%)
Age (years); mean±SD	29.5±6.2	29.7±6.2
BMI (kg/m^2); mean±SD	25.9±4.3	25.4±4.2
Education		
≤ Primary school	3 (3.3)	5(5.6)
High school	37 (41.2)	36 (40.0)
≥ University	50 (55.5)	55 (54.4)
Marital status		
Married	49 (54.4)	48 (53.3)
Cohabitation	38 (42.2)	35 (39.0)
Separated/divorced	3 (3.4)	7 (7.7)
Occupation		
Being unemployed	27 (30.0)	18 (20.0)
Irregular incomer	11 (12.3)	22 (24.4)
Office job	52 (57.7)	50 (55.6)
Primigravida	69 (76.7)	59 (65.6)
Gestational age (weeks); mean±SD	38.5±1.8	38.7±1.8
Duration of operation (minutes); mean±SD	40.2±5.4	40.4±4.1
Blood loss (mL); mean±SD	383.9±33.4	382.2±36.2
Hospital stay (days); mean±SD	4.9±1.4	4.7±1.1

BMI=body mass index; SD=standard deviation

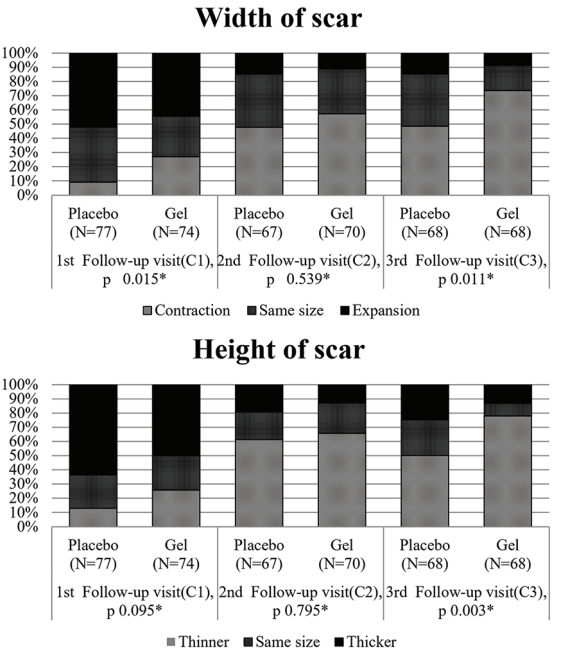

Figure 2. Photograph assessment.

* Fisher's exact test

Table 2. Investigator assessment

	Initial visit (C0); n (%)		1st follow-up visit (C1); n (%)		2nd follow-up visit (C2); n (%)		3rd follow-up visit (C3); n (%)	
	Placebo (n=90)	Gel (n=90)	Placebo (n=77)	Gel (n=74)	Placebo (n=67)	Gel (n=70)	Placebo (n=68)	Gel (n=68)
Redness of scar								
Pale/pink	51 (56.7)	51 (56.7)	19 (24.7)	16 (21.6)	31 (46.3)	34 (48.6)	39 (57.4)	43 (63.3)
Red	21 (23.3)	22 (24.4)	24 (31.2)	17 (23.0)	21 (31.3)	19 (27.1)	16 (23.5)	16 (23.5)
Purple	18 (20.0)	17 (18.9)	34(44.1)	41 (55.4)	15 (22.4)	17 (24.3)	13 (19.1)	9 (13.2)
p-value	1.000*	0.433	0.807*	0.819*				
Surface regularity								
Regular	66 (73.3)	64 (71.1)	38 (49.3	24 (32.4)	31 (46.3)	25 (35.7)	24 (35.3)	12 (17.6)
Medium	18 (20.0)	21 (23.3)	34 (44.2)	24 (32.4)	24 (35.8)	36 (51.4)	30 (44.1)	49 (72.1)
Irregular	6 (6.7)	5 (5.6)	5 (6.5)	18 (24.2)	12 (17.9)	9 (12.9)	14 (20.6)	7 (10.3)
p-value	0.838*	0.009*	0.182*	0.004*				
Attribute of scar								
Smooth	79 (87.8)	74 (82.2)	15 (19.5)	24 (32.4)	26 (38.8)	34 (48.6)	31 (45.6)	46 (67.6)
Medium	5 (5.5)	7 (7.8)	34 (44.1)	26 (35.2)	31 (46.3)	30 (42.8)	28 (41.2)	14 (20.6)
Stiff	6 (6.7)	9 (10.0)	28 (36.4)	24 (32.4)	10 (14.9)	6 (8.6)	9 (13.2)	8 (11.8)
p-value	0.578*	0.183*	0.365*	0.022*				

* Fisher's exact test

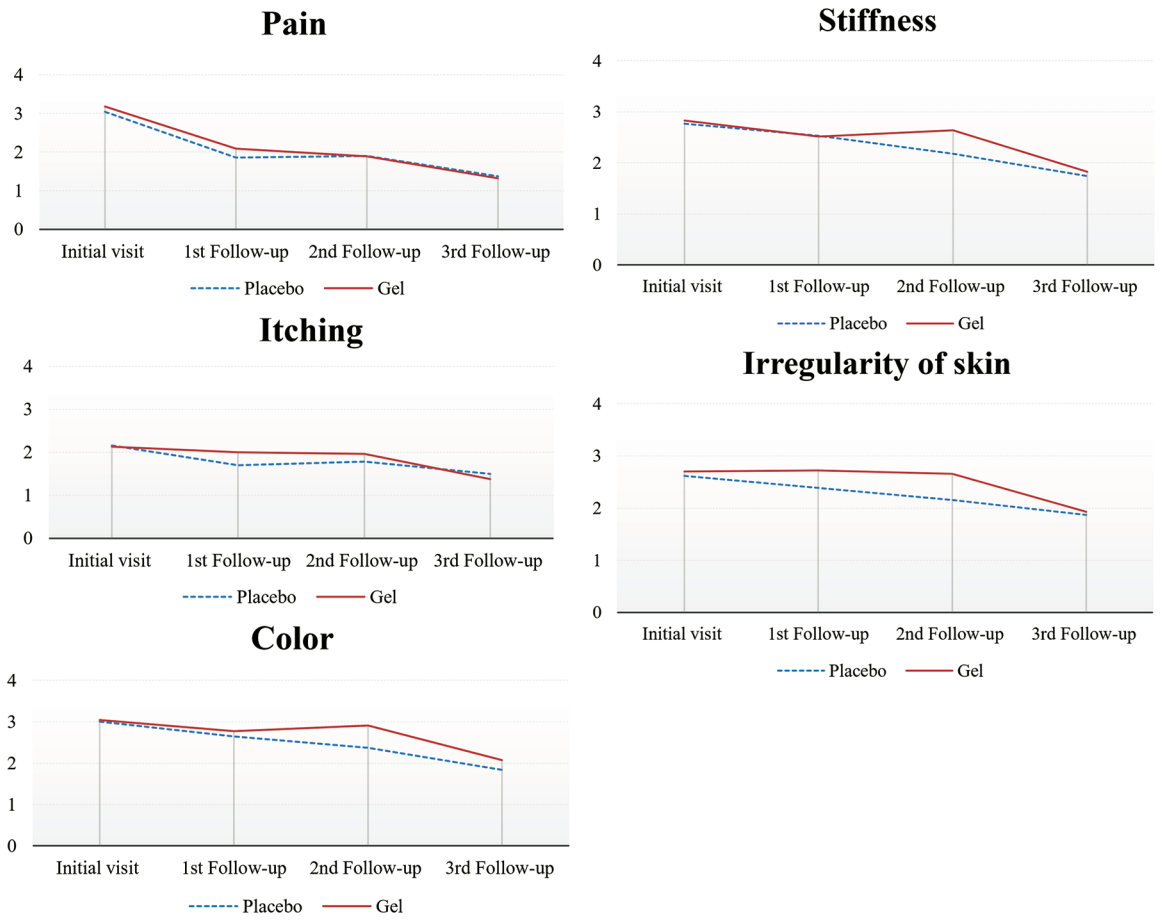

Figure 3. Participants' assessment (score 1=best, 10=worst).

reported 'satisfied' and 49.3% versus 58.8% reported 'very satisfied'.

Discussion

Silicone Pro gel has shown some superiority to placebo gel in terms of scar height, surface regularity, and attribute of scar at three months following a first-time cesarean section. Despite that, there was no significant difference of the participants' wound concerns or satisfaction. This may be due to the fact that motherhood is the first priority in this population, especially in such an early period of their children's lives. However, as permanent scar formation usually starts early and lasts long, the prevention appears pivotal.

Compatible with the previous study by Van de Kar et al[13], patients were more likely to think worse of their scar than the investigators did. The present study shows that although both investigators and patients agreed on the improvement of scar formation, the statistical significance was demonstrated only from the investigators' assessment. Nonetheless, what Van de Kar et al[13] reported supported the high drug compliance of the participants at 80% or more. This underlines the benefit of using scar prevention gel during this period.

Similar to this prospective study, many previous studies demonstrated that topical silicone gel significantly reduced pigmentation, height, and pliability in the management of scars post-operatively compared with placebos or no treatment[14,15]. Moreover, no significant difference was pooled between the topical and the placebo groups for vascularity[14,15].

Regarding silicone gel sheet, topical silicone gel was comparably effective and may be more convenient for patients to use[16,17]. Application of topical silicone gel, together with proper maternal age and lifestyle, would achieve good compliance and treatment efficacy at the same time.

Effectiveness of topical silicone gel and other non-silicone topical treatment such as onion extract was also similar in post-operative scar prevention[17,18]. Combined treatment shown superior efficacy than monotherapy[19]. The combination of herbal extracts and a silicone derivative had been reported to reduce scar development[20]. Further studies should be considered.

The double-blinded and randomized design of this study is the first strength. The preparation of study drug and placebo gel was provided by the same company and its odorless nature minimized reporting bias. Last, all participants who came at each visit finished 80% or more of each tube of study drugs and only a quarter of the participants were loss to follow-up at the end of the study. The limitations included scar formation following cesarean section is apparently multifactorial and rarely pathologic[21]. Surgical technique of closing the wound is as important. All of the participants underwent cesarean section performed by second- or third-year residents, who are in the learning curve of the procedure. The participants can well represent the majority of Thai or Asian pregnant women giving birth by cesarean section at term and the generalizability may also be applied to other East-Asian women due to similar skin type.

Conclusion

Silicone Pro Gel, the unique silicone-based product, has performed better in terms of alleviation of scar development in post cesarean section with high participants' satisfaction. The scar development is one of the major concerns among the women post-operatively in term of the aesthetic reason. According to the evidence of the authors' randomized controlled study, Silicone Pro Gel can be an alternative application to alleviate the scar formation in post-operative cesarean section. Clinicians should select products for each patient while considering both their efficacy and convenience of use. Scar management is an ongoing process over a course of at least three to six months. Therefore, it is essential to ensure patient compliance throughout the medical treatment process.

What is already known on this topic?

There are many modalities using medical or surgical treatment to alleviate scar formation post operatively. Silicone-based products are widely used to limit pathologic scars. Using these products is cost- and time-effective, as well as aesthetic, convenient, and comfortable for the women. To date, a number of clinical trials have assessed the effectiveness, safety, and satisfaction of these products in preventing scars, but have reached no definitive or evidence-based conclusion.

What this study adds?

Numerous silicone-based products are used in modern management of post-operative scars, but this special and unique formula of silicone-based study products, so called " Silicone Pro Gel" has performed better than the placebo in terms of scar alleviation such as scar formation including height, surface regularity, and attribute of the scar. Higher satisfaction was also found among the group of Silicone Pro Gel. Further long-term, large scale, prospective controlled studies are likely warranted to confirm the authors' evidence-based findings.

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Conflicts of interest

The authors declare no conflict of interest.

References

1. Chernoff WG, Cramer H, Su-Huang S. The efficacy of topical silicone gel elastomers in the treatment of hypertrophic scars, keloid scars, and post-laser exfoliation erythema. Aesthetic Plast Surg 2007;31:495-500.
2. Scuderi N, Dessy LA, Buccheri EM, Marchetti F, Mazzocchi M, Chiummariello S, et al. Phase 2 cross-over multicenter trial on the efficacy and safety of topical cyanoacrylates compared with topical silicone gel in the prevention of pathologic scars. Aesthetic Plast Surg 2011;35:373-81.
3. Bock O, Schmid-Ott G, Malewski P, Mrowietz U. Quality of life of patients with keloid and hypertrophic scarring. Arch Dermatol Res 2006;297:433-8.
4. Brown BC, McKenna SP, Siddhi K, McGrouther DA, Bayat A. The hidden cost of skin scars: quality of life after skin scarring. J Plast Reconstr Aesthet Surg 2008;61:1049-58.
5. Chanprapaph K, Tanrattanakorn S, Wattanakrai P, Wongkitisophon P, Vachiramon V. Effectiveness of onion extract gel on surgical scars in asians. Dermatol

Res Pract 2012;2012:212945.
6. Park HJ, Ock SM, Kim HJ, Park HJ, Lee YB, Choi JM, et al. Vitamin C attenuates ERK signalling to inhibit the regulation of collagen production by LL-37 in human dermal fibroblasts. Exp Dermatol 2010;19:e258-64.
7. Meaume S, Pillouer-Prost A, Richert B, Roseeuw D, Vadoud J. Management of scars: updated practical guidelines and use of silicones. Eur J Dermatol 2014;24:435-43.
8. Kim SM, Choi JS, Lee JH, Kim YJ, Jun YJ. Prevention of postsurgical scars: comparsion of efficacy and convenience between silicone gel sheet and topical silicone gel. J Korean Med Sci 2014;29 Suppl 3:S249-53.
9. Wanitphakdeedecha R, Eimpunth S, Manuskiatti W. The effects of mucopolysaccharide polysulphate on hydration and elasticity of human skin. Dermatol Res Pract 2011;2011:807906.
10. Hoeksema H, De Vos M, Verbelen J, Pirayesh A, Monstrey S. Scar management by means of occlusion and hydration: a comparative study of silicones versus a hydrating gel-cream. Burns 2013;39:1437-48.
11. Kwon SY, Park SD, Park K. Comparative effect of topical silicone gel and topical tretinoin cream for the prevention of hypertrophic scar and keloid formation and the improvement of scars. J Eur Acad Dermatol Venereol 2014;28:1025-33.
12. Cromi A, Ghezzi F, Di Naro E, Siesto G, Loverro G, Bolis P. Blunt expansion of the low transverse uterine incision at cesarean delivery: a randomized comparison of 2 techniques. Am J Obstet Gynecol 2008;199:292-6.
13. van de Kar AL, Corion LU, Smeulders MJ, Draaijers LJ, van der Horst CM, van Zuijlen PP. Reliable and feasible evaluation of linear scars by the Patient and Observer Scar Assessment Scale. Plast Reconstr Surg 2005;116:514-22.
14. Kong CG, Kim GH, Kim DW, In Y. The effect of topical scar treatment on postoperative scar pain and pruritus after total knee arthroplasty. Arch Orthop Trauma Surg 2014;134:555-9.
15. Meseci E, Kayatas S, Api M, Boza A, Cikman MS. Comparison of the effectiveness of topical silicone gel and corticosteroid cream on the pfannenstiel scar prevention - a randomized controlled trial. Ginekol Pol 2017;88:591-8.
16. Lin YS, Ting PS, Hsu KC. Does the form of dressings matter?: A comparison of the efficacy in the management of postoperative scars between silicone sheets and silicone gel: a randomized controlled trial. Medicine (Baltimore) 2018;97:e11767.
17. Karagoz H, Yuksel F, Ulkur E, Evinc R. Comparison of efficacy of silicone gel, silicone gel sheeting, and topical onion extract including heparin and allantoin for the treatment of postburn hypertrophic scars. Burns 2009;35:1097-103.
18. Song T, Kim KH, Lee KW. Randomised comparison of silicone gel and onion extract gel for post-surgical scars. J Obstet Gynaecol. 2018;38:702-7.
19. Fang QQ, Chen CY, Zhang MX, Huang CL, Wang XW, Xu JH, et al. The Effectiveness of Topical Anti-scarring Agents and a Novel Combined Process on Cutaneous Scar Management. Curr Pharm Des 2017;23:2268-75.
20. Chuangsuwanich A, Arunakul S, Kamnerdnakta S. The efficacy of combined herbal extracts gel in reducing scar development at a split-thickness skin graft donor site. Aesthetic Plast Surg 2013;37:770-7.
21. Bond JS, Duncan JA, Mason T, Sattar A, Boanas A, O'Kane S, et al. Scar redness in humans: how long does it persist after incisional and excisional wounding? Plast Reconstr Surg 2008;121:487-96.