Biological effects of silicone gel sheeting

LORENZO BORGOGNONI, MD

Since silicone gels were first used in the treatment of hypertrophic scars (HS) and keloids (K) they have proved useful and safe.[1,2] Depending on the specific investigation, the application of silicone gels showed improvements in redness, itching, texture and thickness of HS and K in 60% to 100% of cases[1–14]. Generally, texture was the first scar characteristic to change, followed by color and height[7].

Despite silicone gels wide use in the treatment of HS and K, and the many studies that have been performed in the past 2 decades, the mode of action of these materials remains poorly understood[1]. This knowledge is even more difficult to obtain because the pathogenesis of HS and K is still unclear[2]. Moreover, terms are sometimes used interchangeably, making it difficult to compare results on the effect of treatments among different studies. However, criteria to differentiate HS and K have recently been reported[15,16], and it has been hypothesized that immunologic mechanisms could be involved in the development of HS and K[17–21]. Furthermore, we demonstrated the presence of an immune cell infiltrate in HS and K and characterized the immunophenotypic features of this infiltrate, which are indicative of a delayed type immune reaction[16,22]. HS and K show distinct immunophenotypic profiles, and the amount of the immune cell infiltrate is related to the age and the clinical behavior of HS[22].

It has been reported that silicone gel softens and reduces HS in a shorter period of time than pressure therapy and that the results obtained are not due to pressure, temperature, or oxygen tension[4,5,8,23]. However, it has also been reported that temperature differences of less than 1°C, as found under silicone gel sheeting (SGS), can have a significant effect on collagenase kinetics and may alter scarring[1,24]. Elasticity, measured by elastometry, is significantly increased in SGS treated HS compared with control lesions[8,12].

HS	Hypertrophic scars
IL-8	Interleukin-8
K	Keloids
PDMS	Polydimethylsiloxane
SGS	Silicone gel sheeting

In a recent study, we performed an investigation to evaluate the efficacy of SGS in the treatment of HS and K using objective measurements to confirm subjective evaluations by taking biopsies for histologic and immunohistochemical analysis. Quantitative measures used were thickness using ultrasound and perfusion using laser doppler perfusion imaging. Preliminary results showed a significant reduction of total scar thickness both in HS and in K with SGS treatment. The mean percentage change from the initial assessment of total scar thickness also showed a highly significant reduction. There was a reduction in scar perfusion, although not statistically significant, especially in HS. Biopsies were also taken from patients who at baseline and at 12 weeks had given their consent. We observed a reduction of spindle-shaped cells and an increased number of lymphocytes that strongly expressed CD11a/CD18 (LFA-1) adhesion molecules, which suggests that the SGS application induced modifications of the cell infiltrate in HS and K[25].

It appears there is no release of silicone into the skin after silicone gel application, but this is still not definite. Silicones are synthetic polymers containing a repeating silicone-oxygen backbone and organic groups attached directly to the silicon atom[26]. Elemental silicon is used as a starting material in the manufacture of many silicone products. The most common synthetic polymer is polydimethylsiloxane (PDMS). Depending on the length of the polymer chain and the degree of cross linking, silicone may be differentiated into different classes of commercial products. SGS is composed of gel and a

From the Division of Plastic and Reconstructive Surgery, St. M. Annunziata Hospital, Florence, Italy.
Reprint requests: Dr. Lorenzo Borgognoni, U.O. Chirurgia Plastica, Ospedale S.M. Annunziata, Via Antella 58, 50011 Firenze-ITALIA. Fax: +39 055 2496535; Email: lorenzo.borgognoni@asf.toscana.it.

ISSN: 1067-1927 $15.00 + 0

supporting elastomer membrane. Gels are lightly cross-linked PDMS, where the cross-link is achieved with vinyl and hydrogen groups on separate silicone atoms in the presence of a catalyst. This polymer network is swollen with PDMS fluid to yield a sticky, cohesive mass without form, depending on the extent of cross-linking and on how much fluid is added. Elastomers are composed of PDMS fluid, cross-linked like gel but to a much greater extent, containing very little free fluid polymer. In addition, special forms of amorphous silica compose up to about 30% of its weight[26].

No evidence of inflammation or foreign body reaction in the scars treated with SGS has been reported, suggesting that silicone does not enter the treated tissue[8], and no silica from the dressing was found at the wound site[23]. However, the release of silicone-related compounds from a SGS and their distribution into the skin were shown in vitro[27]. In this case, the silicone-related compounds distributed in the skin might have some pharmacological effects on the tissue.

A possible mechanism of action of SGS could be to bring about occlusion and hydration, which in turn are able to induce modifications in the scar tissue. In fact, it has been shown that SGS induces hydration of the skin surface[28] and occlusion and hydration have a therapeutic action on HS and K[29,30]. However, these effects are obtained with silicone creams/dressings with or without silicone[29–32]. Moreover, it has been shown in vitro that hydration, not silicone, inhibits the proliferation of fibroblasts and their collagen production[33]. After occlusion, an increased number of mononuclear cells were found in the epidermis[34]. It has also been reported that there was an activation of the Langerhans cell system—i.e., Langerhans cells extended their dendrites into the granular layer and made contact with mononuclear cells—and an appearance of Langerhans cells in the dermis after occlusion[2,34,35].

Cytokine mRNA changes have been shown after the treatment of HS with both silicone and hydrogel occlusive dressings. Increased mean levels of interleukin-8 (IL-8),

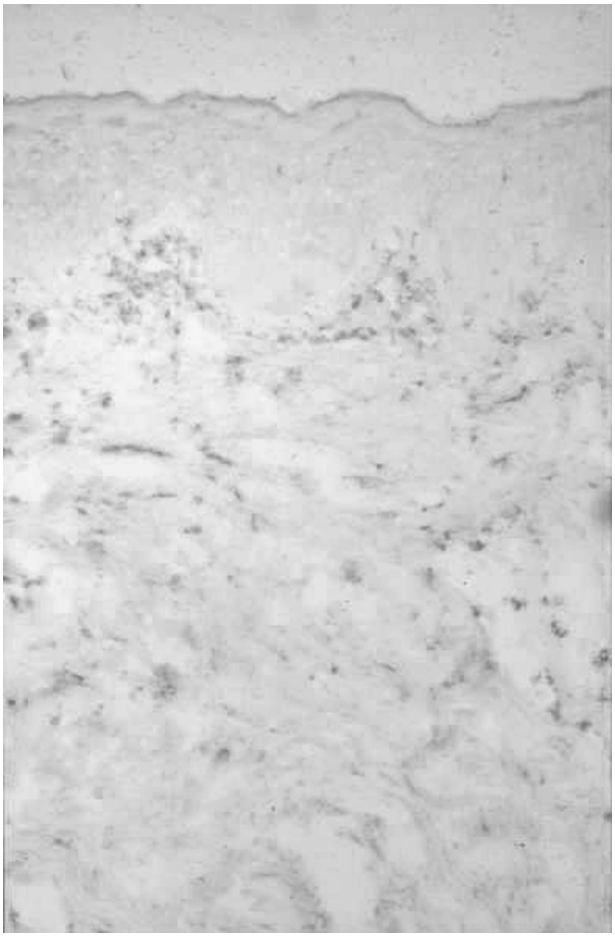

FIGURE 1. A low number of CD68+ macrophages is present in the dermis of the scar three months after keloid excision (APAAP method, original magnification x100).

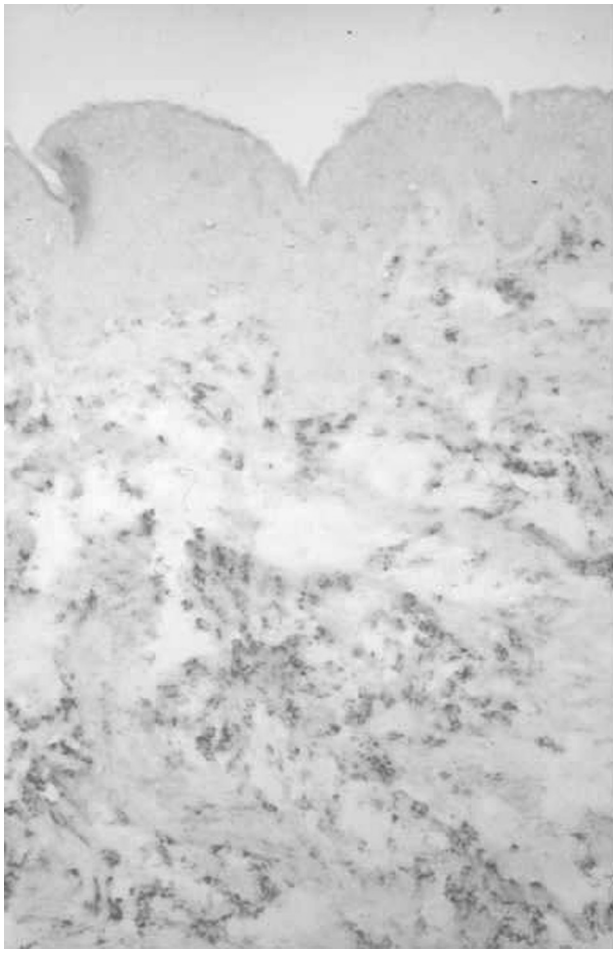

FIGURE 2. A high number of CD68+ macrophages is present in the dermis of the scar after keloid excision and silicone gel sheeting application for three months (APAAP method, original magnification x100).

basic fibroblast growth factor, granulocyte-macrophage colony-stimulating factor and decreased levels of transforming growth factor beta and fibronectin were found after treatment with both dressings. However, only the hydrogel dressing revealed significant changes in IL-8 and basic fibroblast growth factor levels relative to untreated scars. Significant changes in IL-8 and fibronectin were found after treatment with the hydrogel dressing, whereas only fibronectin changes were significant after the treatment with silicone gel sheeting relative to normal skin[36].

Therefore, it seems that occlusion and hydration could have some biological effects on HS and K with or without the use of silicone. However, it is still unclear whether the effects induced by SGS are exactly the same as those induced by hydration obtained by other methods. Silicone could act not only by causing hydration, but also through other mechanisms.

In fact, it has also been reported that static electricity, generated by friction-activated silicone sheeting, helps to cause involution of HS and K[37,38]. Moreover, a silicone cushion, which induces an increased and continuous negatively charged static-electric field, obtained similar effects to SGS and shortened the treatment period in HS and K[39]. It has been hypothesized that the interaction between the negative static-electric field of silicone cushions and the charged components of the tissue fluids could induce the involution process in HS and K[37,39].

SGS has been shown efficacious not only in the treatment but also in the prevention of HS and K. The application of SGS after surgical resection prevented the development of HS and K in 75% to 85% of the cases[1,2,9,23,40–42]. In a previous report[43], we studied a selected group of individuals with K that recurred after a previous surgical excision. One group of patients with these K underwent a further surgical excision and the second group with K were treated with surgical excision followed by the application of SGS for 3 months. In the scars where SGS was applied, we observed a significantly higher rate of complete remission. Moreover, we found a higher number of CD36+ dendritic cells and CD68+ macrophages in the scars treated with SGS when compared with the pretreated lesion and with the scars in which the SGS was not applied (Figures 1, 2), suggesting that SGS application could induce the remodeling processes in the scar tissue.

In conclusion, despite some biological effects of SGS that were reported in previous investigations, further studies are certainly needed to better clarify the mechanism of action of this therapy which, due to its noninvasive, effective, and safe nature, is largely used for the prevention and treatment of HS and K.

REFERENCES

1. Lyle WG. Silicone gel sheeting, Plast Rec Surg 2001;107:272–5.
2. Niessen FB, Spauwen PHM, Schalkwijk J, Kon M. On the nature of hypertrophic scars and keloids: a review. Plast Rec Surg 1999; 104:1435–48.
3. Perkins K, Wallis KA. Silicone gel: new treatment for burn scars and contractures. Burns Incl Therm Inj 1983;9:201–4.
4. Quinn KJ, Evans JH, Courtney JM, Gaylor JD, Reid WH. Non-pressure treatment of hypertrophic scars. Burns Incl Therm Inj 1985;12:102–8.
5. Quinn KJ. Silicone gel in scar treatment. Burns Incl Therm Inj 1987;13(Suppl):S33–40.
6. Ohmori S. Effectiveness of silastic sheet coverage in the treatment of scar keloid (hypertrophic scar). Aesth Plast Surg 1988;12:95–9.
7. Mercer NS. Silicone gel in the treatment of keloid scars. Br J Plast Surg 1989;42:83–7.
8. Ahn ST, Monafo WW, Mustoe TA. Topical silicone gel: a new treatment for hypertrophic scars. Surgery 1989;106:781–7.
9. Ahn ST, Monafo WW, Mustoe TA. Topical silicone gel for the prevention and treatment of hypertrophic scars. Arch Surg 1991;126:499-504.
10. Gold MH. Topical silicone gel sheeting in the treatment of hypertrophic scars and keloids. A dermatologic experience. J Dermatol Surg Oncol 1993;19:912–6.
11. Gold MH. A controlled clinical trial of topical silicone gel sheeting in the treatment of hypertrophic scars and keloids. J Am Acad Dermatol 1994;30:506–7.
12. Carney SA, Cason CG, Gowar JP. Cica-Care gel sheeting in the management of hypertrophic scarring. Burns 1994;20:163–7.
13. Dockery GL, Nilson RZ. Treatment of hypertrophic and keloid scars with silastic gel sheeting. J Foot Ankle Surg 1994;33:110–9.
14. Gibbons M, Zuker R, Brown M, Candlish S, Snider L, Zimmer P. Experience with Silastic gel sheeting in pedriatic scarring. J Burn Care Rehabil 1994;15:69–73.
15. Ehrlich PH, Desmouliere A, Diegelmann RF, Cohen IK, Compton CC, Garner WL, Kapanci Y, Gabbiani G. Morphological and immunochemical differences between keloid and hypertrophic scar. Am J Pathol 1994;145:105–13.
16. Santucci M, Borgognoni L, Reali UM, Gabbiani G. Keloids and hypertrophic scars of Caucasians show distinctive morphologic and immunophenotypic profiles. Virch Arch 2001;438:457–63.
17. Placik OJ, Lewis VL. Immunologic associations of keloids. Surgery 1992;175:185–93.
18. Shetlar MR, Shetlar CL, Hedricks L, Kischer CW. The use of athymic nude mice for the study of human keloids, Proc Soc Exp Biol Med 1985;179:549–52.
19. Kisher CW, Pindur J, Shetlar MR, Shetlar CL. Implants of hypertrophic scars and keloids in to the nude (athymic) mouse: viability and morphology. J Trauma 1989;29:672–7.
20. De Limpens J, Cormane RH. Keloids and hypertrophic scars: immunological aspects. Aesth Plast Surg 1982;6:149–52.
21. Castagnoli C, Stella M, Magliacani G, Alasia ST, Richiardi P. Anomalous expression of HLA class II molecules on keratinocytes and fibroblasts in hypertrophic scars consequent to thermal injury. Clin Exp Immunol 1990;82:350–4.
22. Borgognoni, L, Pimpinelli N, Martini L, Brandani P, Reali UM. Immuno-histologic features of normal and pathologic scars: possible clues to the pathogenesis. Eur J Dermatol 1995;5:407–12.
23. Fulton JE. Silicone gel sheeting for the prevention and management of evolving hypertrophic and keloid scars. Dermatol Surg 1995;21: 947–51.
24. Krieger LM, Pan F, Doong H, Lee RC. Thermal response of the epidermis to surface gels. Surg Forum 1993;44:738–42.
25. Borgognoni L, Martini L, Brandani P, Magini B, Bianchi B, Lascialfari L, Reali UM. Objective measurements used in the investigation of the effects of silicone gel sheeting in the treatment of HS and K. Wound Rep Reg 2000;8:A408. [Abstract]

26. Le Vier RR, Harrison MC, Cook RR, Lane TH. What is silicone? Plast Reconstr Surg 1993;92:163–7.
27. Shigeki S, Nobuoka N, Murakami T, Ikuta Y. Release and skin distribution of silicone-related compound(s) from a silicone gel sheet in vitro. Skin Pharmacol Appl Skin Physiol 1999;12:284–8.
28. Suetak T, Sasai S, Zhen YX, Tagami H. Effects of silicone gel sheet on the stratum corneum hydration. Br J Plast Surg 2000;53:503–7.
29. Sawada Y, Sone K. Hydration and occlusion treatment for hypertrophic scars and keloids. Br J Plast Surg 1992;45:599–602.
30. Bieley HC, Berman B. Effects of a water-impermeable, non-silicone-based occlusive dressing on keloids. J Am Acad Dermatol 1996;1:113–4.
31. Sawada Y, Stone K. Treatment of scars and keloids with a cream containing silicone oil. Br J Plast Surg 1990;43:683–8.
32. de Oliveira GV, Nunes TA, Magna LA, Cintra ML, Kitten GT, Zarpellon S, Raposo Do Amaral CM. Silicone versus nonsilicone gel dressing: a controlled trial. Dermatol Surg 2001;27:721–6.
33. Chang CC, Kuo YF, Chiu HC, Lee JL, Wong TW, Jee SH. Hydration, not silicone, modulates the effects of keratinocytes on fibroblasts. J Surg Res 1995;59:705–11.
34. Lindberg M, Forslind B. The effects of occlusion of the skin on the Langerhans' cell and the epidermal mononuclear cells. Acta Derm Venereol 1981;3:201–5.
35. Mikulowska A. Reactive changes in human epidermis following simple occlusion with water. Contact Dermatitis 1992;4:224–7.
36. Ricketts CH, Martin L, Faria DT, Saed GM, Fivenson DP. Cytokine mRNA changes during the treatment of hypertrophic scars with silicone and nonsilicone gel dressings. Dermatol Surg 1996;22:955–9.
37. Har-Shai Y, Lindenbaum E, Tendler M, Gamliel-Lazarovich A, Feitelberg L, Hirshowitz B. Negatively charged static electricity stimulation as a possible mechanisms for enhancing the involution of hypertrophic and keloid scars. Isr Med Assoc J 1999;1:203–5.
38. Hirshowitz B, Ullmann Y, Har-Shai Y, Vilenski A, Peled IJ. Silicone occlusive sheeting (SOS) in the management of hypertrophic and keloid scarring, including the possible mode of action of silicone, by static electricity. Eur J Plast Surg 1993;16:5–9.
39. Hirshowitz B, Lindenbaum E, Har-Shai Y, Feitelberg L, Tendler M, Katz D. Static-electric field induction by a silicone cushion for the treatment of hypertrophic and keloid scars. Plast Reconstr Surg 1998;101:1173–83.
40. Cruz-Korchin NI. Effectiveness of silicone sheets in the prevention of hypertrophic breast scars. Ann Plast Surg 1996;37:345–9.
41. Neissen FB, Spauwen PHM, Robinson PH, Fidler V, Kon M. The use of silicone occlusive sheeting (Sil-K) and silicone occlusive gel (Epiderm) in the prevention of hypertrophic scar formation. Plast Reconstr Surg 1998;102:1962–6.
42. Gold MH, Foster TD, Adair MA, Burlison K, Lewis T. Prevention of hypertrophic scars and keloids by the prophylactic use of topical silicone gel sheets following a surgical procedure in a office setting. Dermatol Surg 2001;27:641–4.
43. Borgognoni L, Martini L, Chiarugi C, Gelli R, Giannotti V, Reali UM. Hypertrophic scars and keloids: immunophenotypic features and silicone sheets to prevent recurrences. Ann Burns Fire Disasters 2000;13:164–9.