Modified injection technique for improving the treatment of keloids

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To the Editor: Keloids are a specific type of scar that exceeds the original wound boundary and unlikely to shrink spontaneously. Numerous methods for treating keloids have been reported, including surgical resection, radiation, injection, laser therapy, and cryotherapy. However, no single method can ensure a complete cure. Among the reported methods, the intralesional injection of steroids is widely used. A large number of studies have shown that the injection of glucocorticoids combined with 5-fluorouracil (5-FU) into the keloid can soften the texture, reduce the volume, and relieve the associated symptoms.[1] The conventional intralesional injection was routinely performed by directly injecting the drug into the parenchyma through the surface of the keloid in a multipoint manner. However, the significant pain caused by this approach usually affects patient compliance. Moreover, it is difficult to evenly distribute the drug into the firm and tight fibrous structure, which may decrease the therapeutic effect. Accordingly, we modified the technique into a two-step operation, by first injecting into the keloid's base and then injecting into the parenchyma.

Fifty patients with keloid who met the clinical diagnostic criteria and were over 18 years old were included in the study. The exclusion criteria were as follows: (1) patients unwilling to complete the follow-up procedures at the designated time; (2) patients who underwent surgery, radiation, injection, laser, or cryotherapy treatment within the previous 3 months; (3) patients with systemic diseases such as hypertension, diabetes, or immune disorder; (4) patients with infected keloids; and (5) patients with keloids larger than 9 cm^2. In total, 50 patients were allocated equally to either the experimental group or the control group using the block randomization method; the conventional injection technique was performed in the control group, while the modified injection technique was performed in the experimental group. The thickness of keloids was evaluated by ultrasound. The hardness of keloids was assessed by ultrasonic shear wave elastography which showed the results as Young modulus. The patients were asked to rate their pain intensity from 0 to 10 immediately after each injection. Symptom changes and side effects were recorded. As a combination, 0.6 mL 2.5% 5-FU has been added to 5 mL 1% triamcinolone acetonide and then mixed with 1 mL 2% lidocaine. The total mixture dose of 0.2 mL/cm^3 was injected intralesionally. The conventional intralesional injection technique was performed in the control group. In the experimental group, 1/3 of the dose was injected into the keloid base using a 29-G needle, and the other 2/3 of the dose was intralesionally injected 5 min later in a multipoint manner [Figure 1A]. The keloid base was identified by inserting the needle through the adjacent normal skin at an angle of approximately 30° until it reached the base of the keloid, which is softer than the keloid parenchyma and harder than the subcutaneous tissue. Then, the needle was positioned parallel to the skin to release the drug. The procedure was repeated every 3 weeks in each patient. The research was reviewed and approved by the Bioethics Committee of West China Hospital at Sichuan University in China.

One patient with one keloid in the experimental group and three patients with four keloids in the control group were lost to follow-up. A total of 46 patients (67 keloids) were included in the analysis. The keloids in the experimental group were thinned by an average of 2.45 ± 1.19 mm after three modified injections, while the conventional intralesional injections thinned lesions by an average of 1.84 ± 0.97 mm, which were significantly less effective than the modified injections ($P = 0.0125$). Elastic modulus (Young modulus) were reduced significantly more by the injections in the experimental group than in the control group. (95.93 ± 69.10 *vs.* 56.81 ± 33.45 kPa, $P = 0.004$). The pain scores evaluated during the first modified injections were 3.16 points lower than that of the conventional intralesional injections (5.75 ± 0.85 *vs.* 8.91 ± 0.97, $P < 0.0001$). No significant differences in side effects were found between the two groups.

Intralesional injection can effectively introduce drugs into the keloid body. This modified injecting technique achieved a better therapeutic effect than the conventional

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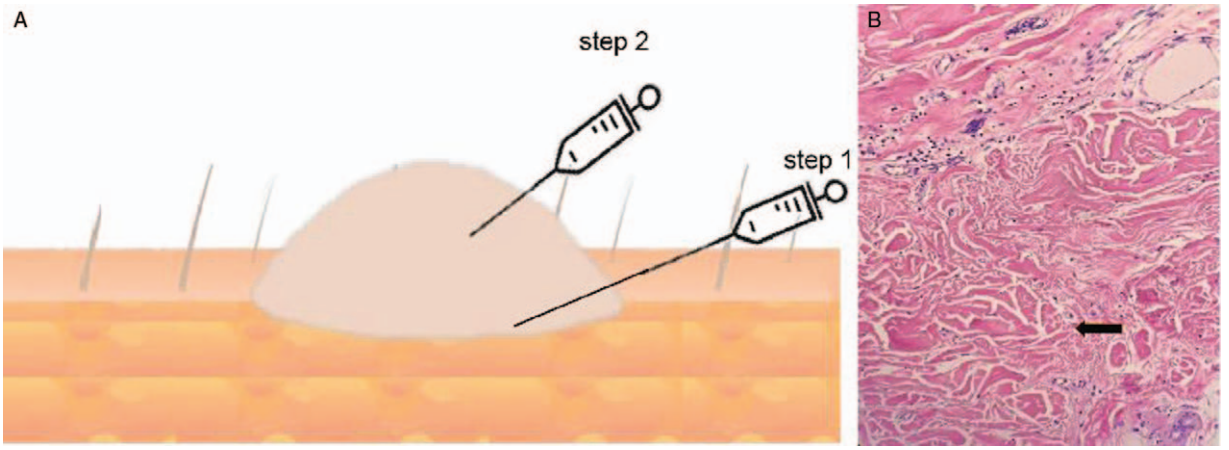

Figure 1: (A) Schematic diagram of the keloid base injection method. (B) Hematoxylin and eosin staining of keloid tissue (original magnification, ×200). The arrow indicates the base of the keloid.

one. With this modified method, the rate of keloid atrophy increased significantly after the injection. The reasons may be related to the following factors: (1) the basal injection facilitated the even distribution of the drug solution. Hematoxylin and eosin staining of the specimen showed that the basal layer of the keloid was much looser than the central part, and the gap between the collagen was large, which is beneficial for the dispersion of the drug [Figure 1B]. (2) The basal injection can directly affect the nourishing blood vessels. The observation of blood flow signals by ultrasound revealed that many hyperactive keloids have significant nourishing vessels at the bottom or near the rim.

Significantly alleviating the pain was another advantage of this modified technique. Due to the firm texture of the keloid, even with the lidocaine added, the conventional injection technique causes severe pain. Many patients in the control group showed a pain index of 8–9 at the first injection. Some methods have been introduced to reduce pain. Ono *et al*[2] used an electronic micropump to inject the drug at a rate of 3 to 6 mL/h. Wang *et al*[3] used surface-freezing anesthesia. By applying the modified injection technique, we inserted the needle precisely into the keloids' base through the normal skin first. The pain intensity was greatly reduced because the collagen density of keloids' base was comparatively lower than that of the parenchyma. With the full effect of lidocaine applied initially at the base, patients would feel little pain when we injected the central part afterward. Menstrual disorders and acne were relatively common in both groups. There are two cases of mild tissue depression in each group.

In conclusion, we demonstrated a modified injection technique which made the injection treatment for keloids more tolerable by reducing pain caused during injections. It could also enhance the effectiveness of injection therapy by increasing keloid atrophy rate.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. On the consent form, the patients gave consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published, and while due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Conflicts of interest

None.

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