The Effect of Microneedle Thickness on Pain During Minimally Invasive Facial Procedures: A Clinical Study

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Abstract

Background: Minimally invasive procedures are becoming increasingly popular because they require minimal downtime and are effective for achieving a more youthful appearance. The choice of needle for minimally invasive procedures can be a major factor in the patient’s comfort level, which in turn affects the physician’s comfort level.

Objectives: In this comparative study, the authors assessed levels of pain and bruising after participants were injected with 30-gauge or 33-gauge (G) microneedles, which are commonly used for minimally invasive injection procedures.

Methods: Twenty healthy volunteers were recruited for this prospective study. Eight injection points (4 on each side of the face) were determined for each patient. All participants received injections of saline with both microneedles in a randomized, blinded fashion. Levels of pain and bruising were assessed and analyzed for significance.

Results: The highest level of pain was in the malar region, and the lowest level was in the glabella. Although all pain scores were lower for the 33-G microneedle, the difference was significant only for the forehead. Because most minimally invasive procedures require multiple injections during the same sitting, the overall procedure was evaluated as well. Assessment of the multiple-injection process demonstrated a significant difference in pain level, favoring the 33-G needle. Although the difference in bruising was not statistically significant between the 2 needles, the degree of bruising was lower with the 33-G needle.

Conclusions: For procedures that involve multiple injections to the face (such as mesotherapy and injection of botulinum toxin A), thinner needles result in less pain, making the overall experience more comfortable for the patient and the physician.

Level of Evidence: 3

Keywords
botulinum toxin A, bruising, microneedle thickness, minimally invasive procedures, pain

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translates to 8.5 million procedures in 1 year. Although some minimally invasive procedures can be executed easily in an office-based setting, certain guidelines must be followed to ensure patient satisfaction and comfort. Complications can occur even when all necessary precautions have been taken.

A primary goal of any injectable procedure is to prevent complications by utilizing safe and proper techniques. Ensuring patient comfort is also of great importance. Because the needles used for such procedures can cause pain, the selection of an appropriate needle is a critical determinant of patient comfort, which in turn affects the comfort level of the administering physician.

The effect of needle thickness on pain has been examined in various studies. The consensus is that reducing needle thickness lowers pain and generally increases the patient’s pain tolerance and satisfaction. However, most of these studies were in diabetic patients, with the goal of achieving higher compliance to insulin treatment. Thus, the areas of injection usually were the abdomen, deltoid, or thigh. A few studies have involved the forearm area of healthy volunteers, but to our knowledge, there have been no studies of the effect of microneedle thickness on pain induced by cosmetic-related injections to the face. Although existing studies provide some insight, they are clinically insufficient and irrelevant as a basis to assess the effect of needle thickness in minimally invasive facial procedures.

Although many products for facial injection contain prepackaged needles, the choice of needle is ultimately determined by the physician. Finer needles are continuously under development, with the intent to further reduce pain and thereby increase comfort during application.

The aim of our study was to investigate and compare pain and bruising associated with 30-gauge (G) and 33-G microneedles when used at common injection sites for minimally invasive facial procedures such as mesotherapy or the administration of botulinum toxin A.

**METHODS**

After obtaining approval of the study protocol from the ethical review board of Gazi University Hospital, 20 healthy adult volunteers from patients presenting to the outpatient clinic were recruited for this prospective randomized study, all of whom provided informed consent.

Study candidates were questioned thoroughly about health issues, medications, and treatments. Candidates with any known illnesses or those under any type of treatment or medication (including vitamin supplements, aspirin, and any analgesic or anticoagulants) were excluded from the study. Age, history of smoking, and history of previous minimally invasive procedures were recorded for all potential participants.

Two frequently used microneedles of different diameters were chosen for comparison in this study. The thicker needle was 30 G (Micro-Fine Plus; Becton Dickinson, Franklin Lakes, New Jersey), and the thinner needle was 33 G (PRE-33013; TSK Laboratory, Oirschot, the Netherlands) (Figure 1). The tapered angle of the tip of both needles was the same (approximately 10°). Both instruments had been used previously in clinical practice by the surgeon who administered all injections in this study (B.S.). Study participants were blinded to the type of needle used for injection.

**Facial Markings and Injection Technique**

Before injection, 4 predetermined injection points were marked on each half (left and right) of the patient’s face: forehead, glabella, midcrow’s feet, and malar area (Figure 2). The point of injection for the forehead was approximately 2 cm above the eyebrow, at the level of the medial canthus. The glabellar injection point was 5 mm above the most medial aspect of the eyebrow. The midcrow’s feet site was 1 cm lateral to the lateral orbital rim, at the level of the...
canthus. The malar injection site was the most prominent point of the malar region.

One of the 2 microneedles was chosen randomly for injection into 1 side of the face; the other microneedle was used on the contralateral side. All participants were injected by the same surgeon, using standard technique. Plain saline (0.05 mL) was injected into each predetermined point, mimicking the administration of botulinum toxin A and other products used for mesotherapy. The injection technique was similar to that for botulinum toxin A, where the most superficial injection was in the crow’s feet. A 45° angle was used for the cheeks, and a 90° angle was used for the glabella and forehead to ensure subdermal penetration. Care was taken to avoid puncturing any visible vascular structures by stretching the skin during injection.

Two parameters, pain level and bruising, were utilized to compare results between the 2 microneedles. Participants were asked to close their eyes during the injection and, shortly afterward, were asked to score their pain level on the visual analog scale from 0 to 10 (0 = no pain, 10 = worst pain ever encountered).

Participants were evaluated the following day for bruising and ecchymosis; evaluation was performed by 2 authors (B.O., H.B.) who had been blinded to the size of the needle. Bruising was scored on a scale of 0 to 2, with 0 representing no bruising, 1 denoting mild bruising (a bruise of <5 mm in diameter), and 2 signifying moderate to severe bruising (a bruise of ≥5 mm in diameter). Bruising was deemed present if ecchymosis was visible on at least 1 side of the face. Therefore, bruising scores were determined for the 2 microneedles overall, not for each area of injection.

**Statistical Analysis**

Pain and bruising scores were analyzed for significance with SPSS for Windows (version 15; SPSS, Inc, an IBM Company, Chicago, Illinois). Mean values and standard deviations were calculated for all data, and results were expressed as mean ± standard deviation. Data analysis was conducted by intergroup comparison of the ranked parameters via the Wilcoxon signed rank test (a nonparametric test for comparing correlated variables). Statistical significance was defined as \( P < .05 \).

**RESULTS**

Ten men and 10 women participated in the study. Mean age was 35.6 years (range, 26-60 years). Eight patients (40%) had a history of smoking, and 9 (45%) had previously undergone minimally invasive procedures. Statistical analysis showed no significant relationship between pain level and age, sex, smoking status, or history of previous procedures (all \( P > .05 \)). No adverse effects occurred from the injections, and all participants experienced only minimal discomfort. Facial markings and clinical results are shown in Figures 3 through 5.

**Pain Scores**

Pain was analyzed with respect to injection location as well as microneedle thickness. The overall pattern of pain sensation was similar for the 2 needles (Figure 6). The comparison of pain between different facial areas showed that the highest level of pain occurred in the malar region (score of 5 ± 2 for the 30-G microneedle and 4.05 ± 1.76 for the 33-G microneedle) and the lowest level in the glabella (score of 2.9 ± 1.8 for the 30-G needle and 2.4 ± 1.5 for the 33-G needle). Pain scores for the forehead were 3.9 ± 1.83 with the 30-G needle and 3 ± 1.55 with the 33-G needle, and those for the crow’s feet were 3.75 ± 1.8 and 3.1 ± 1.48, respectively.

All mean pain scores were lower for the 33-G microneedle (Table 1). With respect to individual injection points, statistical analysis showed that the forehead was the only site where pain was significantly lower with the 33-G needle (\( P < .05 \)). Because minimally invasive cosmetic procedures of the face often require multiple injections, we also examined overall pain levels for the 4-injection process, calculated as the mean pain score of the 2 microneedles for each participant. The mean multiple-injection score was 3.88 ± 1.97 for the 30-G needle and 3.21 ± 1.71 for the 33-G needle. For the 4-injection process, the difference in pain levels between the 2 microneedles was significant, favoring the 33-G needle (\( P < .01 \)).
Figure 3. (A, B) Pretreatment photographs of a 36-year-old woman (A) before and (B) after marking the predetermined injection points. (C) Immediately after injection, via the 30-gauge microneedle on the left side and the 33-gauge microneedle on the right side.
Figure 4. (A, B) Pretreatment photographs of a 26-year-old woman (A) before and (B) after marking the predetermined injection points. (C) Immediately after injection via the 33-gauge microneedle on the left side and the 30-gauge microneedle on the right side.
Figure 5. (A, B) Pretreatment photographs of a 28-year-old woman (A) before and (B) after marking the predetermined injection points. (C) Immediately after injection, using the 33-gauge microneedle on the left side and the 30-gauge microneedle on the right side (which later resulted in a mild bruise at the forehead injection point).
The pattern of pain sensation was similar for the 2 microneedles. The level of pain was highest in the malar region and lowest in the glabella.

Bruising Scores

Bruising was defined as the presence of ecchymosis the day after injection on either side of the face and was scored as minimal or moderate to severe. The 30-G microneedle resulted in minimal ecchymosis at the injection site in 2 patients and moderate ecchymosis in 1 patient. Only 1 patient experienced ecchymosis with the 33-G needle, which was minimal (Figure 5). All ecchymoses occurred in the forehead. Because all injections had been performed by the same surgeon with a standardized technique, bruising was attributed to needle thickness. The mean bruising score was 0.2 ± 0.52 for the 30-G needle and 0.05 ± 0.22 for the 33-G needle (Table 2). Statistical analysis showed no significant difference in bruising between the 2 needles (P > .05).

Patient Satisfaction

After the scoring process was complete, patients were informed of which microneedle had been used on either side of their face. Patient satisfaction was not a primary end point of this study; however, of the 9 participants who had previously undergone minimally invasive cosmetic procedures (such as injection of botulinum toxin A), 7 reported that they would prefer the 33-G microneedle for their next procedure.

DISCUSSION

Minimally invasive procedures such as mesotherapy and injection of botulinum toxin A and soft-tissue fillers are becoming increasingly popular because they require minimal downtime and can achieve a more youthful appearance. Although these procedures are generally simple and reliable, one of the greatest concerns is the injections themselves. The physician’s attitude and the physical environment play important roles in the patient’s comfort level; however, pain, needle phobia, and anxiety can be limiting factors and challenging obstacles for some patients.  

Causes of pain relating to subcutaneous injections have been examined in previous studies, including the needle diameter, bluntness of needle tip, depth of needle insertion, and area of injection.  It has been demonstrated that pain and bleeding can be minimized by careful selection of needles (eg, opting for those with thinner diameters when appropriate) and use of optimal injection angles.  Arendt-Nielsen et al  examined pain and bleeding after injections in the thigh and abdominal region with needles ranging from 23 G to 32 G. Levels of pain and bleeding were significantly lower with the 32G needle in comparison to the other needles used in the study, including a 30G needle, and there was a significant correlation between painful injections and concomitant bleeding. Miyakoshi et al  reported similar results, documenting that abdominal injections with a 33-G microneedle were significantly less painful and resulted in less bruising than a 31-G microneedle.

Although these studies provide valuable information about the effect of microneedle thickness on pain and bruising, they were not conducted in the setting of cosmetic medicine. Only a technical note by Flynn et al  has addressed this issue. In their experience, a 30-G microneedle resulted in little pain. They considered the needle to be an optimal method of delivering precise units of botulinum toxin A to underlying musculature for cosmetic treatment of the aging face. Each microneedle was used only 4 to 6 times to prevent the tip from becoming blunt and causing more pain.

Patients who elect to undergo minimally invasive facial injection procedures differ from those with needle-dependent treatment regimens in that (1) they do not require daily injection and therefore are less accustomed to the injection experience, (2) their procedures usually require multiple injections during the same visit, and (3) their injection process is longer.

To our knowledge, previous studies have not addressed needle thickness in injection sites that are typical for cosmetic facial procedures. With respect to single injections to a given area, our study showed a significant difference in pain only for the forehead, favoring the 33-G needle. The overall pain level associated with the entire procedure also was significantly lower for the 33-G needle. These findings indicate that, with respect to pain, a significant difference exists between a single injection and the multiple-injection process common to many minimally invasive facial procedures. Our results show that, regardless of microneedle thickness, the highest level of pain occurs in the malar region and the lowest level in the glabella.

The properties and volume of the injected fluid are factors that also may contribute to pain during injection, and
these should be taken into account. For example, it has been demonstrated that different approaches to reconstituting botulinum toxin A and the specific types of solution can result in differences in pain sensation. Some physicians use cold compresses, local anesthetic creams, or regional nerve blocks to make the injection process more comfortable. Although these techniques may have limited effects and may introduce certain disadvantages, they can be helpful adjuncts for increasing comfort and reducing apprehension in some patients.

Even though finer microneedles generally result in less pain and greater comfort, they are not suitable for all applications—particularly the administration of products with low viscosity and/or thick formulation, such as soft-tissue fillers. Moreover, very thin microneedles may bend and deform during penetration if they are too long. Therefore, it may be necessary to shorten the length of the needle, which may not permit application to deeper tissue planes. This could be considered a limitation of the present study; the 30-G and 33-G microneedles would not be appropriate for administering fillers of low viscosity. Although these techniques may have limited effects and may introduce certain disadvantages, they can be helpful adjuncts for increasing comfort and reducing apprehension in some patients.

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**CONCLUSIONS**

Multiple factors influence pain tolerance during minimally invasive facial procedures, including the patient’s pain threshold, area and depth of injection, pH, other properties of the substance, and needle thickness. All of these factors must be considered when choosing appropriate microneedles for these procedures. For multiple injections of high-viscosity products to the face, such as botulinum toxin A and injectables for mesotherapy, thinner needles generally result in less pain and bruising, improving the overall comfort of the patient and the administering physician.

**Disclosures**

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