

The Influence of Needle Size on Pain Perception in Patients Treated with Botulinum Toxin A Injections for Axillary Hyperhidrosis

Jette Skiveren¹, Heidi Nordahl Larsen¹, Emmy Kjaerby¹ and Rune Larsen²

¹Department of Dermatology-D42, Copenhagen University Hospital, Bispebjerg Hospital, Bispebjerg Bakke 23, DK-2400 Copenhagen and ²Department of Clinical Immunology, Copenhagen University Hospital Rigshospitalet, Copenhagen, Denmark. E-mail: jski0001@bbh.regionh.dk
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Botulinum toxin A (BTX-A) injections can be an effective treatment for axillary hyperhidrosis, a condition characterized by excessive secretion by the eccrine sweat glands. However, as up to 50 intradermal injections in each axilla are required, the pain experienced by many patients may lead to poor compliance with treatment (1) or to some patients preferring local anesthesia prior to re-treatment (2).

No single effective treatment for pain during treatment with BTX-A has been widely accepted. Topical anesthesia with, for example, tetracaine, is among the most commonly applied methods, but is time-consuming, expensive and often difficult to apply to the axillae (3). Cooling of the skin has also been tested, but with limited success (1). Needle size may also be important. Indeed, small needle size has been associated with a lower frequency of pain in healthy volunteers (4) and in a lower intensity of pain in patients with multiple sclerosis (5). However, other studies have shown pain intensity to be either only slightly affected (6) or unaffected by needle size (7, 8).

Reportedly, injections of BTX-A are typically performed using 27 G (outer diameter 0.4 mm) or 30 G (outer diameter 0.3 mm) needles (1, 9–12). The aim of the present study was to investigate whether the use of a 30 G versus a 27 G needle influenced pain intensity in patients treated with BTX-A for axillary hyperhidrosis.

MATERIALS AND METHODS

Thirty-eight patients (age range 19–48 years, mean 29.1 years) with bilateral axillary hyperhidrosis, 13 (34%) of whom were being treated for the first time, were included in the study. Pregnant women, patients younger than 18 years old and patients with major psychiatric diseases, such as schizophrenia and affective disorders, were excluded. The study protocol was approved by the Scientific Ethical Committee for Copenhagen County (H-D-2007-0059) and conducted in accordance with the Declaration of Helsinki V. All patients gave written informed consent.

The study design was that of a within-patient randomized, controlled trial, with patients acting as their own controls. Coin-tossing and concealed envelopes were used in the randomization procedure.

Patients who regularly shaved their armpits were recommended not to do so within 48 h prior to treatment. Those with hairy armpits had their hair cut to a length of 0.5 cm. Minor's iodine starch test (13) was used to identify the hyperhidrotic area. The borders were marked, and the area divided into 1.5 cm² squares. We used botulinum toxin A (Botox®, Allergan, Irvine, CA, USA) (100 Units diluted in 6 ml of 0.9% sodium chloride). Injections were performed using either 27 G (Micro-

lance® 27G × 3/4" 0.4 × 19 mm) or 30 G (Sterican® 30 G × ½" 0.3 × 12 mm) needles connected to a 3-ml syringe. Needles were inserted at an angle of 20–25°.

Injections were administered intradermally, and the injection volume was 0.1–0.2 ml/1.5 cm². The right axilla was always treated first and the left axilla immediately afterwards. Each patient was treated with a 27 G needle in one axilla and a 30 G needle in the other. Needle size was single-blinded and randomized. Patients were blindfolded to prevent them from seeing the needles. It was not possible to blind the nurse performing the treatment as to which size of needle size was being used. Needles were changed every 20 injections.

Pain was assessed according to a verbal numeric rating scale (NRS), in which 0 represents no pain and 10 the worst imaginable pain. Assessments were performed: (i) just before treatment; (ii) after every five injections; and (iii) immediately after the last injection. The verbal NRS was chosen because immobilization of the patients' arms during treatment prevented the use of a graphical visual analogue scale. In addition, verbal NRS correlate well with conventional visual analogue scales (14). Afterwards, patients were additionally asked to decide whether the treatment administered to the right axilla or left axilla had been more painful. Numbers of injections in each axilla were counted and the total time taken to administer them, including pauses, was recorded.

A reduction in pain score of 2 units on the analogue scale was considered the smallest detectable difference. Based on a test power of 0.80 and a significance level of 0.05, 36 patients were needed to complete the study (Altman's nomogram). We tested the null hypothesis that there would be no difference in pain score between treatments administered using 27 G and 30 G needles. The Wilcoxon signed ranked test for paired samples was used to determine whether changes in pain score were statistically significant. *p*-values of less than 0.05 were considered significant. All analyses were performed using SPSS for Windows (SPSS version 11.51, SPSS Inc., Chicago, USA).

RESULTS

Thirty-eight patients (10 men and 28 women) completed the study. The total time taken to administer the injections, as well as the total number of injections, were similar for the 27 G and 30 G needles (mean 149 vs. 154 s and 31 versus 33 injections, respectively; *n*=38).

Pain scores were on average slightly higher for 27 G needles than for 30 G needles, when all patients were analyzed together as one group (data not shown). However, variability was substantial, and the difference in NRS between the two needles was only statistically significant after the first five injections (*p*=0.038). The highest pain scores were obtained after 15 injections, which, in most patients, were administered to the central parts of the axilla. Dividing the patients into four

Table I. Pain scores (numeric rating scale (NRS)) after botulinum toxin A injections numbers 5, 10, 15 and 20, and after the final injection, in patients treated for relapse of axillary hyperhidrosis and in patients being treated for the first time. Data represent the mean \pm standard error of the mean (SEM).

| Inj. no. | Needle size | Patients treated for relapse (n=25) | | | Patients treated for the first time (n=13) | | | | | |
|----------|-------------|--|--------------|--|--|---|------|---|--------------|------|
| | | 27 G, right axilla (first) 30 G, left axilla (last) n=13 | | 30 G, right axilla (first) 27 G, left axilla (last) n=12 | | 27 G, right axilla (first) 30 G, left axilla (last) n=7 | | 30 G, right axilla (first) 27 G, left axilla (last) n=6 | | |
| | | NRS | Δ NRS | p | NRS | Δ NRS | p | NRS | Δ NRS | p |
| 5 | 27 G | 4.08 \pm 0.54 | 0.39 | 0.51 | 4.58 \pm 0.58 | 0.75 | 0.12 | 3.43 \pm 0.57 | 0.14 | 0.69 |
| | 30 G | 3.69 \pm 0.52 | | | 3.83 \pm 0.47 | | | 3.29 \pm 0.71 | | |
| 10 | 27 G | 5.15 \pm 0.62 | 0.46 | 0.39 | 5.33 \pm 0.45 | 0.5 | 0.36 | 4.29 \pm 0.52 | 0.72 | 0.12 |
| | 30 G | 4.69 \pm 0.44 | | | 4.83 \pm 0.51 | | | 3.57 \pm 0.78 | | |
| 15 | 27 G | 5.46 \pm 0.45 | 0.16 | 0.72 | 5.42 \pm 0.62 | 0.75 | 0.29 | 4.00 \pm 0.69 | 0.00 | 1.00 |
| | 30 G | 5.62 \pm 0.49 | | | 4.67 \pm 0.56 | | | 4.00 \pm 0.93 | | |
| 20 | 27 G | 4.92 \pm 0.43 | 0.46 | 0.21 | 5.08 \pm 0.69 | 0.66 | 0.35 | 3.71 \pm 0.71 | 0.00 | 1.00 |
| | 30 G | 4.46 \pm 0.46 | | | 4.42 \pm 0.61 | | | 3.71 \pm 1.02 | | |
| Last | 27 G | 2.62 \pm 0.56 | | | 4.42 \pm 0.69 | | | 3.14 \pm 0.77 | 0.14 | 0.60 |
| | 30 G | 3.08 \pm 0.73 | 0.46 | 0.26 | 2.92 \pm 0.42 | 1.50 | 0.03 | 3.00 \pm 0.76 | | |

subgroups based on whether they were being treated for the first time or following a relapse, and whether they were treated with the 27 G needle or the 30 G needle first, revealed a tendency towards a more pronounced difference in pain score, in favour of the 30 G needle, but only when the patients were treated with the 30 G needle first (Table I). However, the differences were only significant for the last injections administered. Moreover, these results should be interpreted with caution because of the risk of mass significance and the lack of power due to the small number of patients in each group. In addition, the mean pain scores were, in most cases, higher in patients treated for relapse than in those receiving treatment for the first time.

None of the patients complained of pain before the injections. Nineteen patients (50%) declared that the treatment on the side for which 30 G needles had been used was the more painful and 12 patients (32%) that the side treated using 27 G needles was more painful. Seven patients (18%) felt that there had been no difference in terms of pain between the treatments applied to the right and left axillae.

There were no statistically significant differences between men and women in pain scores for the different numbers of injections and needle sizes ($p > 0.05$).

DISCUSSION

When all patients were analyzed as a group, pain scores recorded after the first five injections were significantly lower for the 30 G needle than for the 27 G needle. However, the difference was only modest and probably too small to be considered clinical relevant (15). Across all the injection series, the mean pain score was, in most cases, above 3.0, which is considered to be the boundary between mild and moderate pain (16). Evidently, however, the pain measured stems not only from perforation of the skin by the needle, but also

from the local delivery of BTX-A solution, which exerts hydrostatic pressure on the surrounding tissue, as well as from the subsequent activation of nocireceptors by chemicals in the solution. Thus, needle perforation may not necessarily be the most important contributor of the pain associated with BTX-A injections, which may, at least in part, explain the limited benefit of using lower-gauge needles.

A number of studies have investigated the influence of needle size on the pain associated with skin injections. However, none of these studies examined the pain associated with injections in the axillae, and it is thus difficult to compare their findings with our results. Moreover, these studies addressed the pain associated with subcutaneous injections, while the injections in our study were administered intradermally.

Of note, the average pain level in the present study was lower than that previously reported by our group in a similar group of patients treated with BTX-A injections using 27 G needles (NRS 5.8 vs. 4.8 and 6.2 vs. 4.8 after 10 and 20 injections, respectively) (1). While, in that study, one injection was administered to every 1-cm² area of skin, the injection area in the present study was 1.5 cm², suggesting that injection area may be of some importance.

That pain scores for both the 27 G and 30 G needles peaked after 15 injections probably reflects local differences in pain sensitivity in the axilla. These injections were administered to more central parts of the axillae, where pain sensitivity seems to be higher, in agreement with our previous findings (1).

The authors declare no conflicts of interest.

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