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Original Article

Evaluation of the Use of PenNeedle® 32G Taper in Children being Treated with Growth Hormone

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Abstract. Pain resulting from needle injection is a serious problem for patients that self-administer medication at home. We studied impressions of needle use by comparing PenNeedle® 32G Taper (NovoFine® 32G Tip), developed to reduce the sense of fear and pain of injection, with a conventional needle, in children self-injecting GH. A total of 34 patients self-injected themselves with needles coupled with Norditropin® NordiFlex® pre-filled recombinant human GH, and impressions of use were evaluated by a series of questionnaires. Compared to the conventional needle, PenNeedle 32G Taper was slightly less painful at time of insertion according to patient responses, though the difference was not statistically significant (P=0.06). PenNeedle 32G Taper has the same inner diameter as the conventional needle, thus there was no difference in the pain felt at time of injection between these two needles. Large differences in pain perception between the two needles were not seen probably due to their similar shape and appearance and as the subjects of this study were young. Nevertheless, based on the results of post-study questionnaires, significantly more patients (68%, P=0.02) expressed a desire to use PenNeedle 32G Taper for daily injections of GH. PenNeedle 32G Taper thus appears to be a superior needle which reduces insertion-associated pain in children receiving recombinant GH and improves patient QOL.

Key words: GH therapy, needle, QOL, pain, self-injection

Introduction

PenNeedles (NovoFine) were developed for self-administered injections of insulin and human GH formulations. Early PenNeedles measured 27G in external diameter and 12.5 mm in length and were used exclusively to inject insulin. In 1993, a needle with an external diameter of 30G and 8 mm in length was launched, followed by the launch of 31G and 6 mm needles in recent years, and they have contributed to improvement in patient compliance. Despite these structural improvements, approximately half of the patients who self-inject human GH formulations were reported to experience pain at the time of injection (1). Pain reduction is thus believed to be important in improving the QOL of patients undergoing GH treatment.

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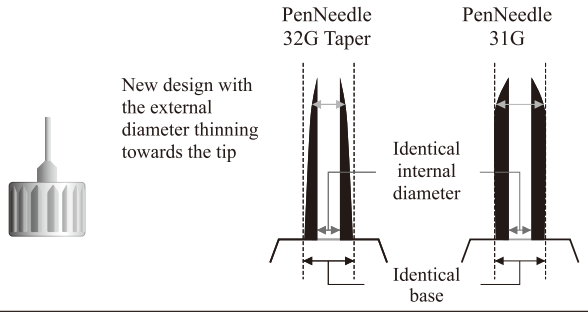


Needle type	PenNeedle 32G Taper	PenNeedle 31G 6 mm
External diameter (mm)	Base 0.25 Tip 0.23	0.25
Length (mm)	6	6

Fig. 1 Pen needle structure / appearance / size of the needle.

PenNeedle 32G Taper released in 2005 was the world's first 32G needle. It was produced by Taper processing and its external diameter gradually thins as it approaches the tip of the needle. This design evolved from the conventional PenNeedle to lower insertion resistance and to reduce injection-associated fear and pain.

In this study, we evaluated the practicality and utility of PenNeedle 32G Taper by comparing impressions of its use with those of a conventional needle (PenNeedle 31G, 6 mm) in children treated with GH using Norditropin NordiFlex 10 mg.

Subjects and Methods

The study included 34 children undergoing self-administered GH therapy with a pen-type, pre-filled human recombinant GH delivery system (Norditropin NordiFlex 10 mg). The study was approved by our Institutional Review Board and informed consent was obtained from both patients and their guardians.

The structures and sizes of PenNeedle 32G Taper and the control PenNeedle 31G, 6 mm are shown in Fig. 1.

This was a crossover study directly comparing patient's impressions on the use of PenNeedle 32G Taper with those on the conventional PenNeedle 31G, 6 mm. To avoid the patients from recognizing the product name, PenNeedles were placed in a small bag, on which the product name was not printed. The product name was printed on the protective tab of the PenNeedle, but as it did not involve any sanitary issues, the protective tab was kept on the PenNeedle. Using a random value table, we assigned numbers for each of the two needles, which were indistinguishable in appearance, and then determined their order of use. The assigned first needle was self-injected by the patient during the first week of the study and then the second needle was self-injected the following week. Each patient completed the "pre-investigation questionnaire" before the study started and a "needle questionnaire" every day during the 2 week study, and a "post-investigation questionnaire" after the completion of the two week investigation, and submitted them to their respective physicians (Table 1).

In order to evaluate the sequential response at the time of injection, a score ranging from 1 point (the best) to 5 points (the worst) was

Table 1 Questionnaire

Respondents
A. Pre-investigation a) Experience of long-term GH therapy b) Number of self-administered GH injections per week c) Impression of GH injections On Scariness (five grades ranging from"very" to "not at all") On Pain (as above) On Trouble (as above)
B. Needle questionnaire (taken daily during investigation) a) Degree of insertion-associated pain (five grades ranging from "very" to "not at all") b) Degree of injection-associated pain (as above) c) Injection-related anxiety (as above)
C. Post-investigation Impressions of the first needle used (free comment) Impressions of the second needle used (free comment) Which needle was more suitable? (choose from: first needle, second needle or no difference between the two) - Less pain - Less pressure for needle insertion - Less bleeding - Fewer liquid leaks - Less pressure needed for injection Which needle do you prefer for daily injection of GH (Choose either first needle or second needle)?

determined for each item, and the average score was analyzed by variance and logistic-regression. Statistical determination of patients' needle preference was performed by mark analysis.

Parents or other adults were allowed to assist children that were unable to complete the questionnaire.

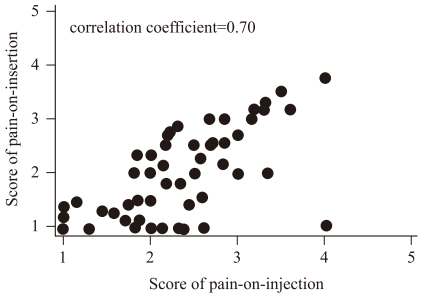
Results

Completed questionnaires were collected from 31 out of 34 (91.2%) patients. Of those, 12 questionnaires were completed by patients alone, 13 by the mother, three by both mother and patient, one by the father, one by another adult, and one by an unknown individual.

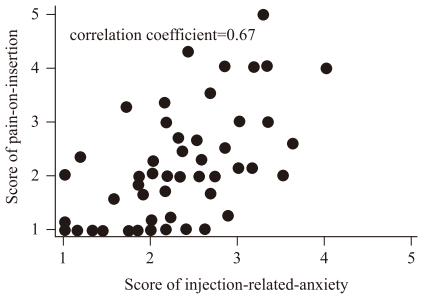
Patients who answered the questionnaires had received GH treatment for an average of 4.6 yr (ranging from 6 mo to 13 yr, median: 2.8 yr). GH injection was prescribed 5 days a week for 7 patients, 6 days a week for 18 patients, and 7 days a week for 6 patients.

The results were not compared by the injection sites, by the person who conducted the injection (self-injection or injection by an adult) or by the time length that the patient had undergone GH treatment.

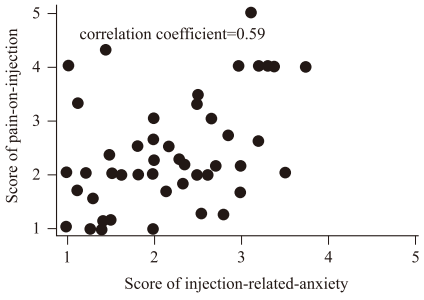
By studying the correlation between each patient's response to the three questions asked before the study, pain associated with GH injection was highly correlated with a sense of fear or scariness (polychoric correlation coefficient=0.80), but not with the perception that injections are troublesome (polychoric correlation coefficient=0.14). Figure 2 shows a scatter matrix of the average scores to the weekly questionnaires for each patient. There was a moderately strong correlation between the three measurements of perception (correlation coefficient = 0.70 between insertion-associated



a. Correlation of the pain-on-insertion and pain-on-injection



b. Correlation of the pain-on-insertion and injection-related-anxiety



c. Correlation of the pain-on-injection and injection-related-anxiety

Fig. 2 Scatter plot of daily scores. Score ranges from 1 to 5 (1=not at all; 5=most).

pain and injection-associated pain, 0.67 between insertion-associated pain and injection-related anxiety, and 0.59 between injection-associated pain and injection-related anxiety).

The responses to the questionnaire regarding the needle were collected sequentially. PenNeedle 32G Taper showed a tendency to be associated with less pain when compared to PenNeedle 31G, 6 mm (31G: 32G Taper, 2.3 ± 0.8: 2.2 ± 0.8, P=0.06), according to the response given to the question on the "degree of pain felt during needle insertion" (Fig. 3). For the pain felt at the time of needle insertion, patients generally tended to mark a lower score (indicating less pain) for the second week than for the first week. No difference in injection-associated pain and injection-related anxiety was seen between the 31G and 32G Taper needles (Fig. 3).

In the post-investigation questionnaire, the majority of patients answered that there were no differences between the two for most parameters when comparing the 32G Taper and the 31G needles. However, 13 patients responded that they felt less pain with PenNeedle 32G Taper (31G: 32G Taper: no difference= 7:13:11 patients). Also, a small number of patients associated the 32G Taper needle with "less bleeding", "fewer liquid leaks", and "less pressure needed during injection" (Fig. 4).

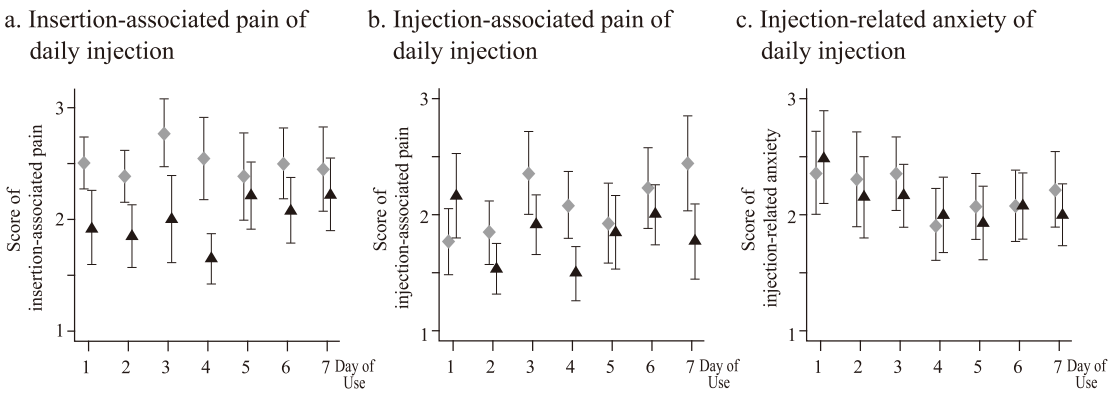
Significantly more patients (68%) chose the 32G Taper over the 31G (Fig. 5, P=0.02) when asked which needle was preferred for daily injection of GH.

Discussion

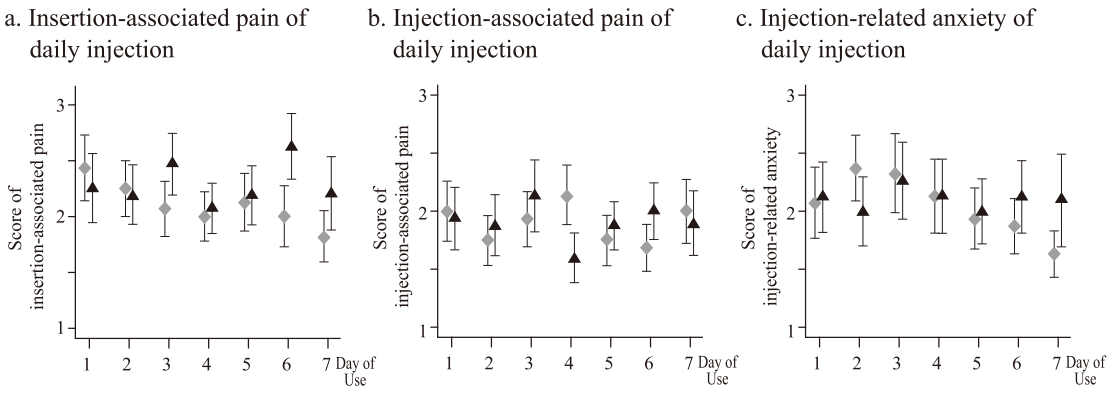
Improving the ease of needle use and decreasing associated anxiety directly increases the QOL of patients that undergo self-administration treatment and reduces the burden on supporting family members. Half of patients experience significant pain during injection, therefore, pain reduction is an important treatment target (1).

PenNeedle 32G Taper has an external diameter of 31G (0.25 mm) at the base of the needle, which Tapers to 32G (0.23 mm) at the tip, and has the same internal diameter as the 31G needle. Although the 32G Taper needle tip is narrow, its base strength, injection resistance and drug outflow time shows no difference with that of a 31G needle (2).

Arendt-Nielsen *et al.* reported a decrease in



The group of patients who used PenNeedle 31G in the first week and PenNeedle 32G Taper in the second week. (n=16)



The group of patients who used PenNeedle 32G Taper in the first week and PenNeedle 31G in the second week. (n=15)

Fig. 3 Sequential change in response to injection. Score ranges from 1 to 5 (1=not at all; 5=most). ▲PenNeedle 32G Taper, ◆PenNeedle 31G. Mean ± S.E.

injection-associated pain as needle size decreased from 30G to 31G and from 31G to 32G (using the 32G Taper 6 mm needle) in 30 healthy volunteers (3). Larger gauges did not show such trend, as Hanas *et al.* reported two trials with no difference in pain perception in double-blinded, randomized comparisons of 27G, 28G, 29G, and 30G (outside diameter ranging from 0.4 mm to 0.3 mm) needles in children (N=60) and teenagers (N=40) with diabetes (4).

For adult patients receiving insulin treatment, evaluation of the use of PenNeedle 32G Taper compared to 31G has been reported in Japan. Nakamura *et al.* reported that 93.2% of the patients were satisfied with the 32G Taper and that 90.9% of the patients said that they would prefer to continuously use the 32G Taper (5). Katayama *et al.* reported that compared to 31G, 32G Taper had significantly lower frequency and degree of pain and significantly more patients were satisfied with it (6). However, no such report has been published for patients on

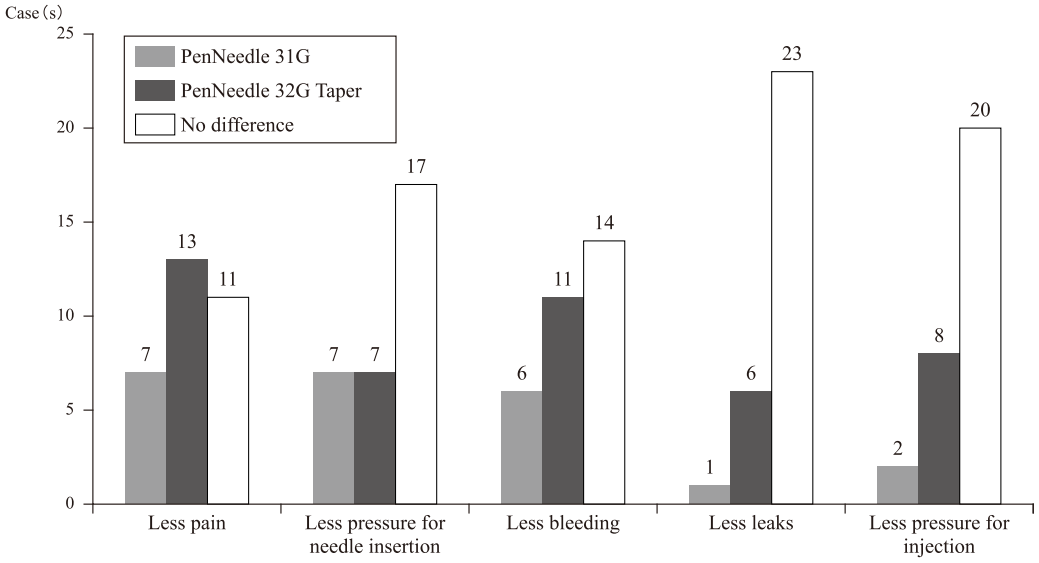
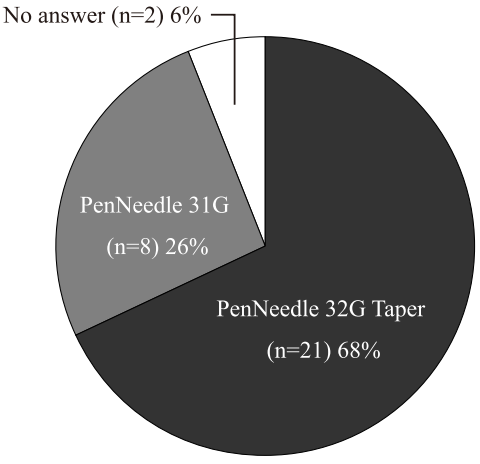


Fig. 4 Results of the questionnaire undertaken on completion of the study—comparison between PenNeedle 31G and PenNeedle 32G Taper.



* Patients showed a significant preference for the PenNeedle 32G Taper (P=0.02).

Fig. 5 Which needle do you prefer for daily injection of GH? (Choose either first needle or second needle) (n=31)

recombinant human GH. In this study we investigated the difference in pain reception in Japanese children on recombinant human GH with the same injection system to avoid obtaining results affected by the use of different systems.

In this study, there were moderately strong correlations between insertion-associated pain and injection-associated pain and between insertion-associated pain and injection-related anxiety (Fig. 2). Increases in the insertion-associated pain have an impact on the patient's compliance, thus it is important to consider reducing the pain at the time of needle insertion and at the time of injection.

Since this study targeted children and because both needles were similar in appearance [the 32G (31G at the needle base) needle is the same length and only slightly thinner (0.02 mm at the needle tip) than the control 31G needle], we thought the results would show no significant difference. However, PenNeedle 32G Taper was associated with less insertion-associated pain, and a large proportion of patients (68%) preferred PenNeedle 32G Taper over the control needle.

In this study, we have received the following comments from the patients, "There was pain as the injection involves the needle pulling the skin", and "As the injection button is stiff and difficult to press, pressure is applied at the time of injection which causes pain"; and from one

patient's mother, "If I could inject smoothly, there might be no pain." Some patients experienced bleeding and complained of pain each day and several commented that there was less pain when the needle was inserted into the skin smoothly. In contrast, higher pain was perceived when the patient felt resistance upon needle insertion.

According to reports on needle use and insulin self-injection, it is not the thinness of the needle but the thinness of the internal diameter that increases the infusion pressure and affects the injection-associated pain. The 31G and 32G Taper needles used in this study have the same internal diameter, thus there was no difference in infusion pressure. This is reflected in our results in which there was no difference in injection-associated pain between the two needles. In addition, since the needles were nearly identical in appearance, injection-related anxiety, a parameter that can be influenced by its appearance, showed no difference between the two needles (Fig. 3). There was some bleeding upon injection for both 32G Taper and 31G needles, but there was no incidence of tip breakage during the study. There are some concerns that the tip may break upon injection, but we hope for improvement in this area.

The patients in this study experienced less pain in the second week compared to the first week, which may indicate that the patients had become desensitized to injections. However, because this investigation was performed in a group of patients who had already experienced extensive injection treatment and because there was no decrease in score for each period, this was unlikely to have been a significant contributing factor (Fig. 3).

We considered that expectation of the investigation (i.e. needle to be used in the 2nd week is better than the 1st week) would affect the scores, but there was no correlation between the preferred needle and the needle used in the second week.

From this study, it can be concluded that the PenNeedle 32G Taper is a superior needle that reduces the insertion-associated pain in children and improves the patient's QOL when it is used in combination with Norditropin NordiFlex.

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