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Clinical Testing Results and High Patient Satisfaction with a New Needle-Free Device for Growth Hormone in Young Children

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Fifty children ages 4–10 yr with type 1 diabetes mellitus volunteered to participate in a study to evaluate and compare a new needle-free device developed for growth hormone delivery. Children answered descriptive questions related to nervousness and worry, hurt or pain, redness or bleeding, and stinging and wetness. Choices for answers for each of these five questions were none, a little, or a lot. None or a little was also combined to give a minimal category. Children also answered four questions that compared the needle-free device to their morning insulin needle injection in reference to ease of use, pain, nervousness, and overall preference. Half the children had single comfort rings inserted to increase the injection pressure. Results indicated no difference in question responses with or without pressure rings. Pain (92%), erythema (96%), worry (90%), stinging (86%) and wetness (96%) were minimal and significant ($0.001 > p < 0.03$) following all questions. Results of the comparative questionnaire indicated that the device was easier ($p < 0.03$) to use than needles and significantly preferred ($p < 0.001$) in 74% of children under age 10.

Key Words: Needle-free; type I diabetes mellitus; GH.

Introduction

Drug delivery with the use of a needle-free device is an alternative method that provides comparable bioavailability to a needle and syringe for the administration of growth hormone (GH) but has improved patient comfort and acceptability *(1–4)*. Recently, needle-free delivery has been utilized to deliver GH using a safe and effective needle-free device in adults and children *(1–7)*. The results to date suggest that this needle-free device is preferred by more than 70% of adults and teenagers compared to needles and is equally acceptable to patients receiving GH in pen devices *(3,5,6)*.

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In spite of a number of studies using needle-free devices, few have focussed on young children *(5,6)*. Our studies look specifically at children less than 10 yr of age with type 1 diabetes mellitus using the new cool.click® (Bioject, Portland, OR) needle-free device *(7)*. Young children with diabetes mellitus were chosen as subjects because of their knowledge and experience with daily insulin injections.

Results

Adverse reactions in 50 children included only minimal bleeding that was easily controlled by mild pressure with gauze or cotton balls. There was no evidence of hematoma or bruising and no visible skin lacerations that have been described with older needle-free devices *(8–10)*.

In the descriptive questionnaire, highly significant differences favoring the absence of redness, stinging, apprehension, pain, and wetness occurred after a single needle-free administration of saline using the needle-free device (Table 1). Results from Questions 1–5 showed no significant differences between one and no comfort rings with device A and B, respectively. Regarding Question 5, there were two more occurrences of wetness without any comfort rings, but this was not statistically significant. Regarding Question 1, 38% of the children had no fear or worry, 52% had a little fear or worry, and 10% were very worried. Therefore, with the needle-free device, minimal worry (none or a little) constituted 90%, which was significantly ($p \leq 0.001$) more common than the very worried (10%). Pain or discomfort from the needle-free device was absent in 52%, slight in 40%, and severe in 8%. Minimal pain occurred in 92%, which was significantly ($p \leq 0.01$) more likely than severe discomfort. Redness or erythema was absent in 70%, slight in 26%, and prominent in 4% of subjects using the needle-free device. Minimal erythema or bleeding occurred in 96% of young children and was significantly ($p \leq 0.01$) more common than prominent local reactions. Stinging was absent in 66% of children, slight in 20% and frequent in 14%. Therefore, stinging was minimal in 86% of young children and more common ($p \leq 0.03$) than severe stinging. Wet injections, defined as a small drop of liquid, at the injection site following saline administration were uncommon, with 84% noting none, 12% a little, and 4% (or two patients)

Table 1
Answers to Descriptive Questionnaire

Question		No	A little	Minimal	Severe (Very)	Total	*p*
1	Device A[a]	10	13	23	2	25	0.99
1	Device B[a]	9	13	22	3	25	
	Total			45[b]	5	50	
Question				Minimal	Severe (A lot)	Total	*p*
2	Device A	15	9	24	1	25	0.609
2	Device B	11	11	22	3	25	
	Total			46[b]	4	50	
Question				Minimal	Severe (Very)	Total	*p*
3	Device A	18	7	25	0	25	0.490
3	Device B	17	6	23	2	25	
	Total			48[b]	2	50	
Question				Minimal	Severe (A lot)	Total	*p*
4	Device A	19	2	21	4	25	0.99
4	Device B	14	8	22	3	25	
	Total			43[b]	7	50	
Question				Minimal	Severe (Very)	Total	*p*
5	Device A	22	2	24	1	25	0.99
5	Device B	20	4	24	1	25	
	Total			48[b]	2	50	

[a] Needle-free device; A = one ring; B = no ring.
[b] Difference between minimal and severe is $p \leq 0.01$.

with splashback (more than one drop). Therefore, 96% ($p \leq 0.01$) of subjects experienced minimal wetness with the needle-free device.

Figure 1 summarizes the results of the preference questionnaire. Sixty-six percent ($p \leq 0.03$) of the children indicated that the needle-free device was easier to use. Although the majority of the young children were more afraid of needles (62%) and found them more uncomfortable (60%), these differences were not statistically different. However, 74% of young children ($p \leq 0.001$) overall preferred the needle-free device to conventional needle injections.

Discussion

Needle-free administration of GH is bioequivalent to needle injections and equally acceptable to patients using a needle injection device *(1–7)*. Previous studies with the needle-free device in an older group of children, ages 11–18 yr, showed similar acceptance using similar descriptive and preference questionnaires. However, in this older group, 76% of children experienced more pain and discomfort with needles ($p \leq 0.01$) than the needle-free device *(5, 6)*. In addition, the older children appeared significantly more nervous with their first needle-free administration compared with the younger children in this study *(6)*.

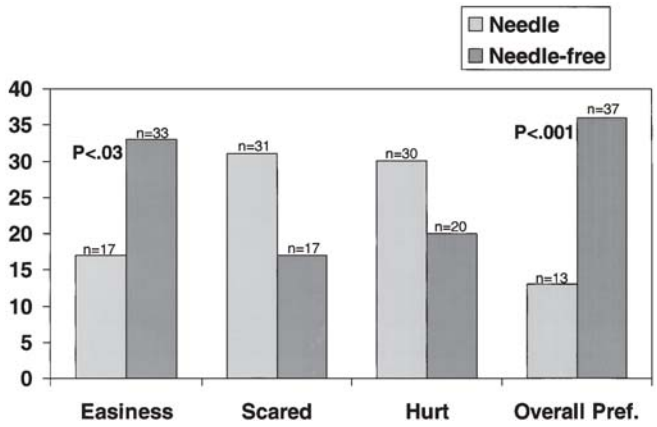

Fig. 1. Comparison of needle and needle-free injection regarding ease of use, fear or worry, hurt or pain, and overall preference. The vertical axis indicates the number of responders.

In the past, adverse reactions with needle-free administration have demonstrated large hematomas and bruising lasting up to 3–5 d *(8–10)*. By contrast, a newer needle-free device reported in the present study and elsewhere *(5–7)*, has demonstrated either no adverse reactions or minimal bleeding easily controlled with mild pressure.

In this study, we found that with young children, needle-free administration was safe to use, generally well tolerated, and strongly accepted and preferred by almost all patients. Clinical studies in children with type 1 diabetes mellitus showed a dichotomy in their preferences based on age. Prior to their first administration, older children found that the needle-free device increased their nervousness over needle injection, yet they subsequently rated needle-free administration as clearly less painful, equally convenient and overall preferred to needle injections *(5,6)*. Children age 10 yr and under (74% of subjects) clearly preferred the needle-free device and found it significantly easier than needle injections.

Materials and Methods

Study Protocol

Fifty children ages 4–10 yr and their parents or guardians signed consent forms for an Institutional Review Board approved protocol by The University of Florida Institutional Review Board (Gainesville, FL). Children were attending Camp Study Programs in March and August 2000 at the Florida Camp for Children and Youth with Diabetes. Part of this study was previously reported elsewhere *(6)*. All children had diabetes mellitus and were taking insulin injections using 28 to 30-gage disposable needles and syringes. Half of the children tested received devices with no comfort rings and half received devices with one large comfort ring. Injection pressure with the cool.click® device can be adjusted utilizing comfort rings. A comfort ring is thought to reduce wet (one or more drops of liquid) injections. One

of the goals of the study was to assess for any differences in rate of wet injections and sensation with and without comfort rings.

The descriptive questionnaire requested answers based on a single, needle-free administration of saline (0.9% Normal Saline USP) regarding the presence or absence of nervousness and/or worry, hurt or pain, redness or bleeding, stinging, or wet injections. In the comparative questionnaire, children or children and their parents were asked to compare a single, needle-free administration of saline with the previous morning's insulin needle injections. Children were given the choice of sites (arm, thigh, or stomach) of administration and could either self-administer or receive an administration from the study nurse. Questionnaires were answered shortly after their needle-free administration to ascertain patient acceptability and preference.

Analysis of Questionnaire Data in Children with Diabetes Mellitus

Fifty children <10 yr old with type 1 diabetes were subjects in two questionnaires comparing the needle-free device to a needle and syringe for the administration of insulin. All subjects were asked a series of nine questions. The first five questions concerned their reactions to or perceptions of the needle-free device:

1. Did you feel worried or scared?
2. Did the injection hurt?
3. Was it red where you injected?
4. Did the injection sting?
5. Did the injection feel wet?

The last four questions compared the needle-free device to a needle and syringe and asked which they would prefer to use every day:

1. Which would be easier to use?
2. Which would make you more scared or worried?
3. Which hurt more?
4. Which would you like more?

The data for the first five questions had a three-point scale representing none, a little, and a lot or very much. To simplify the statistical analysis, those subjects responding with either none or a little were combined in one category called minimal. Prior tests of subjects using a needle have confirmed the presence of slight pain and unpleasantness in using a needle *(5,6)*. The larger difference between minimal and severe pain or unpleasantness is of interest in assessing the needle-free device for acceptance by subjects. The presence of any of the five sensations to a severe degree was deemed to be undesirable, and, therefore, the scale was collapsed into minimal and severe. The difference between minimal and severe was then tested to determine whether a severe level of pain or unpleasantness for these five sensations was reported by these 50 subjects.

Fisher exact test was used to test for differences between needle-free devices with the two comfort settings, which were labeled as device A (one comfort ring) and device B (no comfort rings) on the case report form and in Table 1 *(11)*. The results of the tests showed no significant differences between the settings for all nine questions. Because the tests failed to reject the hypothesis of independence between the device used and the answer to any of the nine questions, the data for the two devices were combined for analysis purposes.

The combined data were tested for significant differences at the $\alpha = 0.05$ level, two sided, against the null hypothesis proportion of one-half (0.5) using the binomial distribution *(12)*. The *p* values for all tests/comparisons are given in Table 1.

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