

Original Article

Clinical Evaluation of the Needle-free Injection System VISION[®] for Growth Hormone Therapy in Children

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Abstract. The aim of this study was to compare the therapeutic effects of rhGH administered either by subcutaneous needle-injection (pens) or subcutaneous needle-free jet-injection (VISION[®]). Furthermore, a survey was carried out after using VISION[®] for 12 mo. A needle-free injection group consisting of 18 subjects (11 males and 7 females, mean age 5.87 ± 2.05 yr at the start of hGH therapy) who have not used pen injectors to date, were allowed to use VISION[®] in their third to fifth years of GH therapy. In addition, a group of 8 subjects who had been using pen injectors at our clinic (6 males and 2 females, mean age 6.54 ± 2.78 at the start of GH therapy) was monitored as a control. The results indicate that there are no significant differences between the mean growth rates, growth rate SD scores or height SD scores when comparing injection devices. Furthermore, the survey of VISION[®] revealed that 70% of the subjects found it slightly or not painful at or after injection, 70% found VISION[®] very easy or easy to use, and 80% found the weight of the device appropriate. All subjects expressed a desire to continue using VISION[®] in the future. Our results suggest that there are no problems with the effectiveness of hGH treatment with VISION[®], a needle-free jet-injection device and that VISION[®] is an effective device for children who have an aversion to needle injection.

Key words: GH deficiency, GH therapy, Needle-free jet-injection device

Introduction

Syringe materials have changed from glass to plastic, while the shape of the syringe itself has not changed much. The biggest change, has been in the size of the needle. In particular, needles have become thinner, reaching the present size of 32 gauge.

On the other hand, new syringe design has been sought. In order to eliminate the fear, pain

and infection of needle injection, needle-free injection systems have been designed and put into clinical use.

Needle-free injection devices used in Japan include the Twin-Jector EZ and EZ II for human growth hormone use, SYRIJET for dental surgery/surgical management, and ShimaJET, recently developed and commercialized by a Japanese company for insulin use.

Several studies have compared needle-free injectors to conventional syringes with needles. So far, the results have been conflicting: the needle-free injector has been reported to be both less painful and more readily accepted by the patients and their families than conventional needle injection (1, 2), while other reports found

Received: February 24, 2006

Accepted: May 25, 2006

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no differences between needle-free injection and conventional syringes (3).

In 1993 we investigated the use of a needle-free injection system for GH therapy and reported that it was beneficial in improving patients' adherence to treatment regimes and that no differences were found in the therapeutic effects, compared with needle injection (4). In our clinic, we carried out GH therapy using a needle-free injector for children who feared needle injection. However, due to a product recall in November 2000, an alternative needle-free injection system, VISION[®], was imported directly from ANTARES PHARMA Co., U.S.A. and used for GH therapy.

We have collected data from 18 subjects using the VISION[®] needle-free injector and 8 subjects using conventional needle pen-injectors, and compared the data. Furthermore, a survey of the VISION[®] users was carried out. The results are reported below.

Subjects and Methods

The needle-free injection (VISION[®]) manufactured by Antares Pharma Co. is shown in Fig. 1. The needle-free syringe was exchanged with a new one, once a week.

A needle-free injection group consisting of 18 subjects (11 males and 7 females, mean age 5.87 ± 2.05 yr at the start of hGH therapy) who

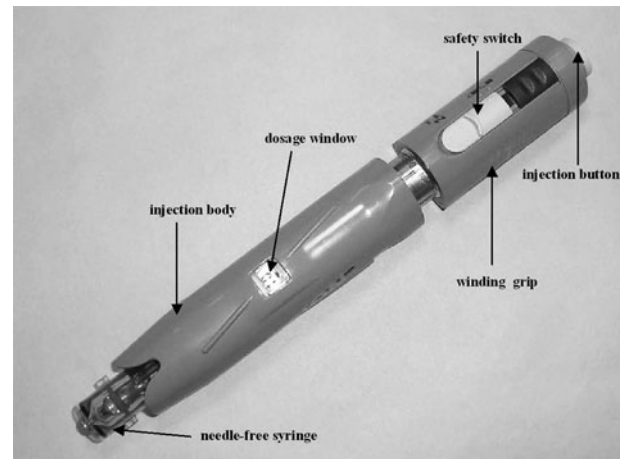


Fig. 1 Needle-free injection device, VISION[®].

have not used needle injectors to date, were allowed to use VISION[®] in their third to fifth years of GH therapy. In addition, a group of 8 subjects who had been using needle injectors at our clinic (6 males and 2 females, mean age 6.54 ± 2.78 at the start of GH therapy) was monitored as a control (Table 1). All subjects were pediatric patients with GH deficiency (GHD).

Growth rates, growth rate SD scores and height SD scores from the needle-free injection group were compared with the control group and evaluated. Numerical values are shown as mean \pm SD. Using the t-test, probabilities of not more than 5% were determined as significant difference.

Table 1 Patient background of needle-free injection group and needle injection group

Parameters	Needle-free injection group	Needle injection group
Number of subjects	18	8
Male to female ratio	11:7	6:2
Chronological age at start (yr: decimal notation)	5.9 ± 2.0 (18)	6.5 ± 2.8 (8)
Height at start (cm)	98.6 ± 10.7 (18)	100.7 ± 14.4 (8)
Height age at start (yr: decimal notation)	3.8 ± 1.5 (18)	4.2 ± 2.2 (8)
Height SD score at start (SD)	-2.9 ± 0.5 (18)	-3.1 ± 0.7 (8)
Growth rate at start (cm/yr)	4.9 ± 1.0 (18)	5.5 ± 1.6 (8)
Growth rate SD score at start (SD)	-2.2 ± 1.2 (18)	-1.1 ± 1.9 (8)
Weight at start (kg)	15.6 ± 4.7 (18)	15.2 ± 5.3 (8)
Gestational age (wk)	38.1 ± 9.6 (17)	38.4 ± 20.3 (5)
Birth weight (kg)	2.6 ± 0.9 (18)	2.5 ± 1.4 (5)

Table 2 Survey contents

- Did you have pain at injection?
- Did you have pain after injection?
- In comparison with injection by former needle-free injector,
 - (1) were you able to easily understand how to use VISION®?
 - (2) were you able to easily inject with VISION®?
 - (3) did you find the size of VISION® appropriate?
 - (4) did you find the weight of VISION® appropriate?
- Do you wish to continue using VISION®?

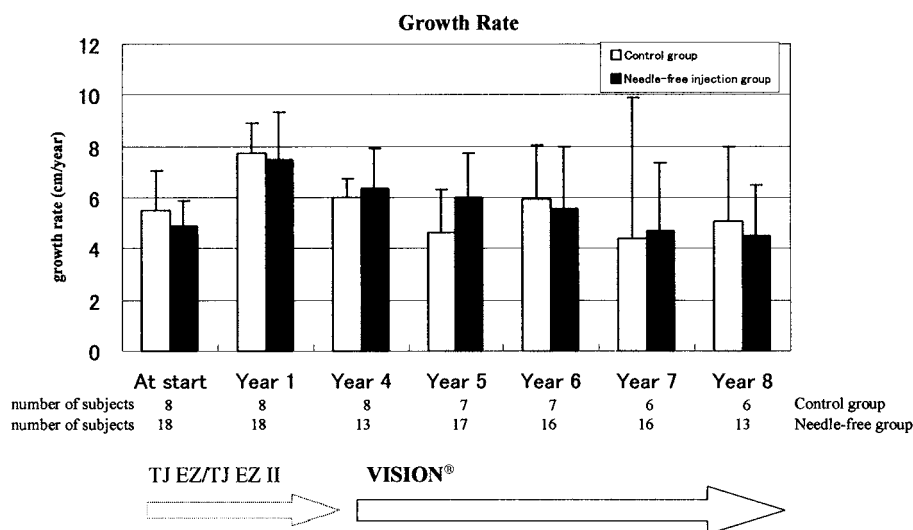


Fig. 2 Mean (SD) growth rates during duration of treatment by needle-free injection or traditional needle injection.

A survey was carried out after using VISION® for 12 mo (Table 2), in which the operation and effectiveness of the device were evaluated.

Written consent to participate in this survey was obtained from the parents of the patients.

Results

For each parameter, as shown in Table 1, no differences were observed in the backgrounds of the needle and needle-free groups of patients.

Figure 2 shows growth rates. The growth rates for both groups over 8 yr from the start of GH treatment were compared, with no significant differences observed between the needle and the

needle-free groups. Figures 3 and 4 show growth rate SD scores and height SD scores, respectively. No differences were observed between the two groups in either the growth rate SD scores or the height SD scores.

The survey was given to the 18 subjects who had experienced needle-free injection using Twin-Jector EZ, Twin-Jector EZ II and/or VISION®. Answers were obtained from 17 subjects (6 girls and 11 boys). The response rate was 94.4%. Figures 5–9 show pain at injection, pain after injection, how to use, size/weight and desire to continue use, respectively. At injection, 70% felt slight or no pain. After injection, approximately 70% felt no pain. In comparison with the previous

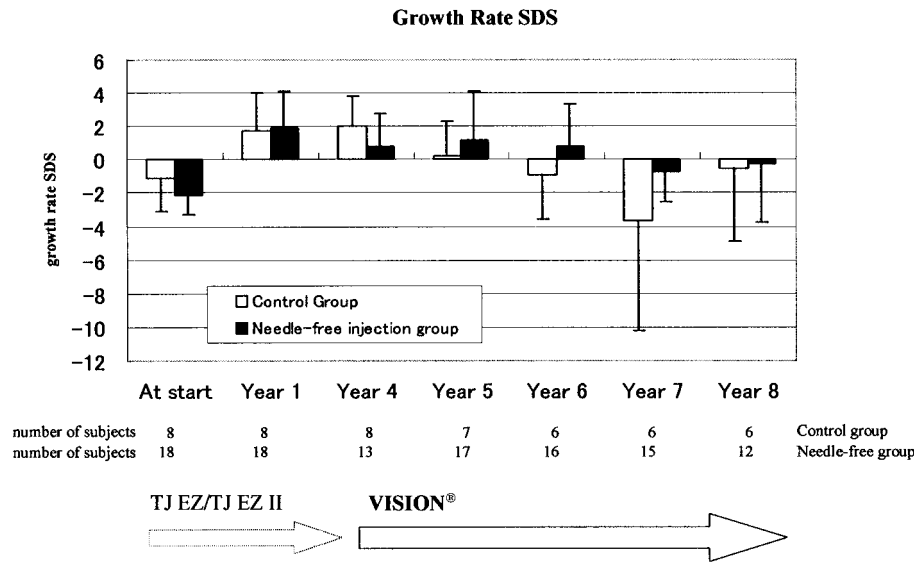


Fig. 3 Mean (SD) growth rate SD scores during duration of treatment by needle-free injection or traditional needle injection.

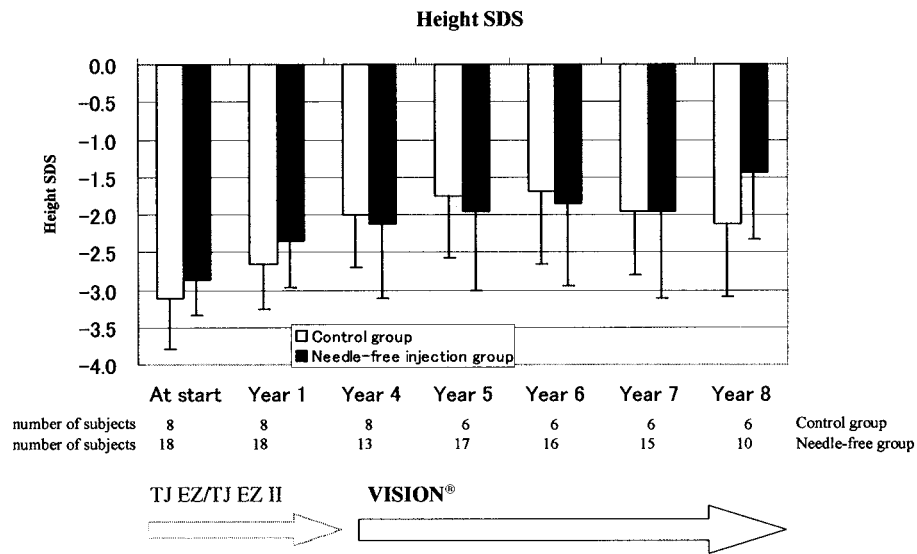


Fig. 4 Mean (SD) height SD scores during duration of treatment by needle-free injection or traditional needle injection.

needle-free injectors, Twin-Jector EZ and/or Twin-Jector EZ II, about 70% responded that the directions for use of VISION were easy or very easy to understand. They also found that VISION® itself was easy to use. The subjects found the VISION injector to be appropriately sized and easy

to handle. In addition, 80% or more answered that VISION® was not heavy. All subjects expressed a desire to continue using VISION in the future.

Regarding breakage, in 4.5 yr of use by 18 subjects, a total of 3 syringes were broken by 2 subjects at our clinic. All incidents occurred at

●Did you have pain at injection?

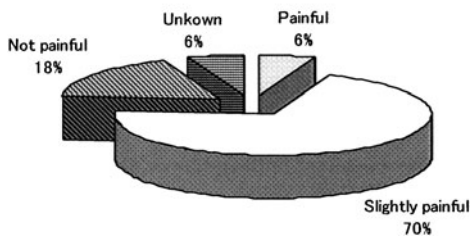


Fig. 5 Responses to the descriptive questionnaire after using the needle-free injection (VISION®) for 12 mo.

●Did you have pain after injection?

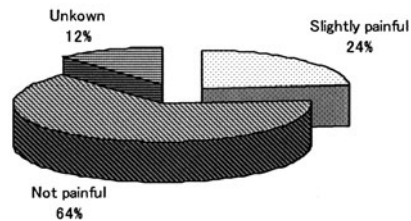
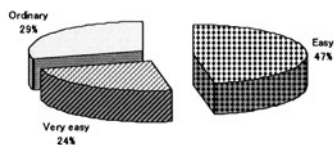


Fig. 6 Responses to the descriptive questionnaire after using the needle-free injection (VISION®) for 12 mo.

(1) Directions on how to use VISION



(2) Ease of injection with VISION

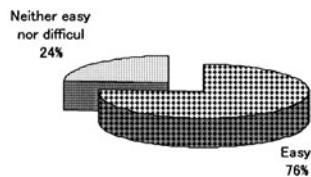
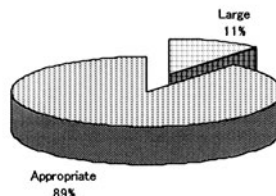


Fig. 7 Responses to the descriptive questionnaire after using the needle-free injection (VISION®) for 12 mo.

(3) Size of VISION



(4) Weight of VISION

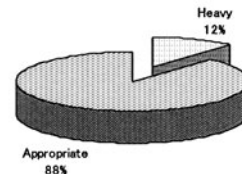


Fig. 8 Responses to the descriptive questionnaire after using the needle-free injection (VISION®) for 12 mo.

the initial stage of using VISION® and could have been caused by inappropriate operation.

Discussion

GH deficiency was treated by intramuscular injection of GH extracted from human pituitary glands in the early 1960s. Since then, there have been many advances in treatment encompassing administration, the injection product and the injection device.

In our clinic, we use a pen needle device for

●Do you wish to continue using VISION?

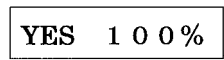


Fig. 9 Responses to the descriptive questionnaire after using the needle-free injection (VISION®) for 12 mo.

the treatment of GH. But the needle-free alternative is an effective solution for children who have an aversion to needle injection, and it

is useful for increasing the dose of GH treatment.

In the United States, VISION® has been approved for subcutaneous self-administration of insulin by insulin-dependent diabetes mellitus patients. In Europe, VISION® (ZomaJect 2) has been used for subcutaneous self-injection of growth hormone.

Several studies have been carried out comparing pharmacokinetic and pharmacodynamic characteristics of needle-free systems with traditional needle injection (5–9). These studies support the use of jet injection as a viable alternative to the traditional injection pens with needles.

This study was designed to compare the therapeutic effects of rhGH administered by subcutaneous needle-injection (pens) with subcutaneous needle-free jet-injection (VISION®). The results showed that no significant differences were found in the growth rates, growth rate SD scores or height SD scores, when comparing injection devices. Furthermore, the survey of VISION® revealed that 70% found it slightly or not painful at or after injection, 70% found VISION® very easy or easy to use, and 80% found the weight of the device appropriate.

As for complaints on using VISION®, only 3 syringes were damaged by 2 subjects in 4.5 yr of use of VISION®. All breakages occurred at the initial stage of using VISION® and could have been caused by inappropriate handling. Subsequently, there was no breakage observed up to the end of study. There were no other complaints. Therefore, it was concluded that there are no problems regarding safety and operationality for hGH treatment with VISION®, a needle-free injector.

The results indicate that there are no problems regarding effectiveness of the VISION® needle-free injector for hGH treatment. The results also indicate that VISION® is an effective device for children who have an aversion to needle injection.

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