Multicenter Study on Clinical Evaluation of Disposable Syringes Pre-loaded with Growth Hormone (Genotropin KabiQuick)

Seizo Suwa, Katsuhiko Tachibana, Yoshihide Ohyama, Masatoshi Fujimoto, Osamu Shinohara and Etsuro Tokuhiro

Department of Pediatrics, Kanagawa Children's Medical Center (S.S., K.T.), Kitasato University (Y.O.), St. Marianna University (M.F.), Tokai University (O.S.), Odawara City Hospital and Yokohama City University (E.T.), Kanagawa, Japan

Abstract. A short term multicenter study on evaluation of the usefulness, acceptability and tolerability of Genotropin KabiQuick (GKQ) was carried out in 36 patients with classical growth hormone (GH) deficiency. Of 36 patients or their parents, 32 (88.9%) evaluated GKQ as superior in preparative procedure to the conventional injection syringe system. Thirty (83.3%) including all of the 6 self-injection patients evaluated that dosing with GKQ was easier. Thirty-two (88.9%) said that GKQ could be handled in a more sanitary condition. Twenty-six (72.2%) felt that the handling of GKQ was easier. The average time needed for each injection with GKQ was 4.0 ± 3.2 min. which was significantly shorter than that with the conventional system (7.8 ± 6.2 min). Ten, twelve and thirteen patients complained that GKQ gave more, equal and less pain respectively. Nineteen (52.8%) commented that the plunger of GKQ was hard to push. Twenty-two (61.1%) preferred GKQ and 5 (13.9%) reverted to the conventional system for future treatment. Doctors concerned with this study assessed that GKQ was useful in 27 patients (75%), but not useful in 2 patients (5.6%). It is concluded that GKQ is an easy handling device which provides quick, safe and sterile daily injections for patients or parents, but an easily movable plunger, a smaller size device and a lower dose-system GKQ are requested for further improvement.

Key words: Genotropin KabiQuick, all-in-one injection system, growth hormone, growth hormone deficiency, KabiPen

Introduction

The utilization of human growth hormone (GH) is rapidly increasing in the treatment not only of GH deficient children (GHD) but also of other short children such as those with Turner's syndrome, because of its wider availability. Daily subcutaneous injections

Correspondence: Dr. Seizo Suwa, Kanagawa Children's Medical Center, Hospital for Sick Children, 138-4 Mutsukawa 2-chome, Minami-ku, Yokohama 232 Japan.

This study was supported in part by grants from the Ministry of Health and Welfare, Japan and by a research grant from the Foundation for Growth Science in Japan.

of GH are reportedly more effective than the same weekly dose given intramuscularly divided into two or three doses [1-4]. Recently it has been common practice for GH to be self-injected at home. Therefore, there is a strong need to simplify the methods of administration. However, the conventional procedure of GH injection using a needled syringe and vial is considered inconvenient for patients and parents, because the procedure needs the reconstitution of vial GH powder with ampuled diluent, and the re-transfer of an adequate dose of GH solution into the syringe for each injection. Therefore several devices for injection such as pocket injection pens [5,6] have been developed to provide an easier injection system for patients to cope with daily injections at home. But these injectors still require several troublesome procedures or specific GH vials containing preservatives. Recently a more convenient all-in-one single use injection system, Genotropin KabiQuick (GKQ), has been developed [7]. This system consists of a single use disposable injection syringe and special holder which encloses a two-compartment cartridge (one compartment for GH powder and the other for dilution water) as a mixing device for reconstitution. GKQ holds pre-prepared GH in a cartridge (2, 3 or 4 IU) for a single injection, hence GH solution contains no preservative.

The aim of this study was to evaluate the usefulness, acceptability and tolerability of the new injection system in patients with GHD.

Subjects and Methods

The patients

Thirty-six patients with classical GHD (5 from Yokohama City University Hospital, 3 from Odawara City Hospital, 7 from Kitasato University Hospital, 5 from St. Marianna University Hospital, 5 from Tokai University Hospital and 11 from Kanagawa Children's Medical Center) were enrolled in this study. Twenty-nine of them were idiopathic in

nature (27 boys, 2 girls) and 7 organic (4 boys, 3 girls).

The patients ranged in age from 6.1 years to 19.3 years (mean 12.6 years), and had been treated with GH for 3.5 years in average (range from 2 months to 12.5 years). The weight of the patients ranged from 15.3 kg (9.3 years, boy) to 55.0 kg (16.9 years, boy) and averaged 35.0 ± 11.0 kg. The height ranged from 106.4 cm (6.1 years, boy) to 157.4 cm (16.0 years, boy) and averaged 136.3 ± 15.8 cm. At the time prior to the study, the patients received recombinant GH (4 or 12 IU Genotropin per vial) of 0.45 ± 0.07 IU/kg/week in average, generally injected subcutaneously divided in 4-7 (mean 5.9 ± 1) doses using a conventional disposable needled insulin syringe.

The injection syringe

The all-in-one disposable syringe, Genotropin KabiQuick (GKQ) was used. Of the three kinds of dose-system of GKQ preloaded with a cartridge containing 2, 3 or 4 IU of recombinant GH powder in one compartment and 0.5, 0.75 or 1 ml water for reconstitution in another compartment respectively, a single dose-system was selectively or two kinds of dose-system were alternatively used for one patient. Selection of the dose-system of GKQ depended upon the patient's body weight and number of injection times per week.

The person responsible for injection

Six patients performed self-injection, 28 were injected by a parent during the study. Two patients were alternatively injected by themselves or a parent.

The study protocol

The conventional syringe system was replaced with the GKQ system, and GH treatment was continued without any change of dose and injection times per week. The trial

Evaluation of Genotropin KabiQuick

Table 1. Patient's evaluation of preparative procedure with Genotropin KabiQuick compared with the conventional injection system

person responsible for injection	more convenient	equal	less convenient
patient	4	2	0
pt. and parent	2	0	0
parent	26	2	0
total	32 (88.9%)	4 (11.1%)	0

Table 2. Patient's evaluation of facility in handling of Genotropin KabiQuick compared with the conventional injection system

person responsible for injection	easier	equal	more difficult
patient	3	3	0
pt. and parent	2	0	0
parent	21	6	1
total	26 (72.2%)	9 (25.0%)	1 (2.8%)

was conducted as an open study between December 1991 and January 1992. The study period in each patient was between 1 and 4 weeks. Before the start of the study, demonstrations and instructions in the function and using technique of the GKQ were given to each patient and/or parent by a doctor, and the patient and parent practised using the injector at a regular visit to the out-patient clinic. Informed consent was obtained from all patients and/or parents before the study. For evaluating the new injection system, a questionnaire with 9 items was completed at the end of the study either by the patient and/or the parent, depending on the age of the patient and the type of question posed.

Results

Of 36 patients or parents, 32 (88.9%) evaluated that the preparative procedure with Genotropin KabiQuick (GKQ) such as reconstitution of GH, needle attachment and expiration of air from the syringe was more convenient than that with the conventional syringe injection system (Table 1). Four patients or

Table 3. Patient's impression on sanitary condition in handling of Genotropin KabiQuick compared with the conventional injection system

person responsible for injection	more sanitary	equal	less sanitary
patient	5	1	0
pt. and parent	2	0	0
parent	25	3	0
total	32 (88.9%)	4 (11.1%)	0

Table 4. Patient's evaluation of facility in dosing with Genotropin KabiQuick compared with the conventional injection system

person responsible for injection	easier	equal	more difficult
patient	6	0	0
pt. and parent	1	1	0
parent	23	5	0
total	30 (83.3%)	6 (16.7%)	0

Table 5. Time consumed for each injection

		Minutes(M $\pm$ SD)
Genotropin KabiQuick	(N 34)	4.0 $\pm$ 3.2
conventional injection	(N 34)	7.8 $\pm$ 6.2

parents found the two systems equally convenient, and none expressed GKQ was less convenient. Twenty-six (72.2%) felt that the handling of GKQ was easier than the conventional system, but 9 felt it equal to it and only one more difficult (Table 2). Thirty-two (88.9%) had an impression that the sanitary condition in handling GKQ was superior to the conventional system (Table 3). Thirty (83.3%) of 36 patients or parents including all of the 6 self-administration patients answered that dosing with GKQ was easier than with the conventional system but 6 thought there was no difference between the two systems (Table 4). The average times consumed for each injection including preparative procedure are shown in Table 5. The time needed for the GKQ system was significantly shorter ($p < 0.05$) than that for the conventional system.

Ten (27.8%), 12 (33.3%) and 13 (36.1%) patients complained that injection by GKQ gave more pain, equal pain and less pain than

Table 6. Patient's complaint of injection pain by Genotropin KabiQuick compared with the conventional injection system

person responsible for injection	injection pain		
	more	equal	less
patient	0	3	3
pt. and parent	0	1	1
parent	10	8	9
total	10 (27.8%)	12 (33.3%)	13 (36.1%)

Table 7. Patient's free comments on inferiority of Genotropin KabiQuick to the conventional injector

complaints	No. of patients or parents
hard to push the plunger	19 (52.8%)
occupies more room for keeping	5 (13.9%)
hard to remove air in GH solution	5 (13.9%)
hard to watch the plunger	2 (5.6%)

the conventional injection respectively (Table 6).

Inconveniences of GKQ were arbitrarily pointed out by patients or parents as shown in Table 7. Nineteen patients or parents (52.8%) commented that the plunger of GKQ was hard to push and hence a longer time was needed to inject the solution. Five (13.9%) complained that GKQ occupied more room for storage in the refrigerator, and the other 5 that it was not easy to remove the air or bubble in the reconstituted GH solution in the syringe. Other comments such as difficulty in watching the plunger (2 parents), heavy weight (1 parent) and difficulty watching the needle (1 patient) were pointed out as inferiorities of the GKQ compared with the conventional syringe.

Patients or parents were asked to state their own choice of injection system, GKQ or the conventional injection, for future treatment, and their answers are listed in Table 8. Twenty-two (61.1%) preferred GKQ and 5 (13.9%) the conventional system, but 9 (25%) gave non-committal answers. The reasons why the patients or parents preferred the conventional injection system to GKQ are listed in Table 9.

The usefulness of GKQ for each patient

Table 8. Patient's preference for future use

person responsible for injection	preference		
	KabiQuick	non-committal answer	conventional syringe
patient	3	3	0
pt. and parent	2	0	0
parent	17	6	5
total	22 (61.1%)	9 (25.0%)	5 (13.9%)

Table 9. Reasons why Genotropin KabiQuick was not preferred for future use

reasons	children
hard to push plunger + more pain	3
hard to push plunger	1
more pain + more room for storage	1

Table 10. Doctor's assessment on usefulness of Genotropin KabiQuick for each patient

assessment	No. of patients
useful	21 (58.3%)
a bit useful	6 (16.7%)
equal to the conventional syringe	7 (19.4%)
not useful	2 (5.6%)

was assessed by the physician in charge as shown in Table 10. GKQ was assessed as useful in 21 patients (58.3%), somewhat useful in 6 (16.7%), and not useful in 2 (5.6%). The last 2 patients refused to use GKQ for future injections because of pain.

Discussion

It has been reported that pocket injection pens such as KabiPen [5-7] or Nordject [8,9] are more convenient than the conventional syringe injection system for patients or parents. But the injection-pen system has some inconvenient problems as follows: the procedure for dissolving GH and setting a vial into the pen needs several steps, dose adjustment is necessary for each injection, GH solution which is intended for multi-dosing injection contains preservative and the weight of the pen is too heavy. Genotropin KabiQuick

Evaluation of Genotropin KabiQuick

(GKQ) was devised to eliminate the time-consuming procedure of reconstitution, vial setting and dose setting, and most of the patients in this study expressed the opinion that GKQ was more convenient in the preparative procedure than the conventional injection system and the dosing adjustment procedure was unnecessary. The time consumed for each injection by GKQ was about half of that for the conventional system. Most of the patients or parents reported that they were able to handle GKQ in a more sanitary condition than the conventional syringe-vial system. About two-thirds of the patients said that handling GKQ was easier than that of the conventional syringe and vial system, but more than half of the patients complained that the plunger of GKQ was hard to push. About one third of the patients complained that GKQ gave a stronger injection pain than the conventional syringe injection, but another one third reported that the pain was less. Injection pain with GKQ was caused presumably by the difficulty in pushing the plunger.

About two-thirds of the patients or parents preferred GKQ to the conventional injection system, but 5 families disliked the new device because of the hard moving plunger and stronger pain.

Using one or two kinds of dose-system of GKQ, all of the patients who ranged in weight between 15 and 55 kg were able to be treated with GH of about 0.5 IU/kg/week. The 9.6-year-old boy with the lowest body weight (15.3 kg) was injected with 2 IU GKQ 4 times per week (8 IU/week = 0.52 IU/kg/week), and the 16.9-year-old boy with the heaviest weight (55.0 kg) was injected with 4 IU GKQ 7 times per week (28 IU/week = 0.51 IU/kg/week). However, a lower dose-system, such as 1 IU GKQ, is thought to be necessary for younger patients with a body weight of less than 15 kg.

These data obtained from the patients in this study are consistent with another report [10]. The doctors who were concerned with this study assessed that GKQ was a useful injection system for most of the patients, and

it is concluded that GKQ is a new easy handling device which may provide quick, safe and sterile daily home-injections for non-professional persons and may allow more children to take responsibility for their own therapy. But there remains some room for further improvements such as an easily movable plunger, a smaller size device and a lower dose-system.

Acknowledgement

We express great thanks to Sumitomo Pharmaceutical Co., Ltd. (Osaka, Japan) for supplying Genotropin KabiQuick.

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