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Blood Glucose and Free Insulin Levels After the Administration of Insulin by Conventional Syringe or Jet Injector in Insulin Treated Type 2 Diabetics

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Summary

The levels of blood glucose and free insulin were compared in 20 diabetic subjects (type 2) receiving one dose of a combination of fast-acting and intermediary-acting insulins in the morning by means of a needle syringe or a jet injector (SICIM, Italy), using minimum possible injecting power. A shift to the left in the free insulin profile, consequential to different pharmacokinetic characteristics of insulin when administered by means of a jet injector, was observed, although no significant differences were seen for free insulin levels. Statistically significantly higher blood glucose values ($P < 0.05$) were recorded 6 and 9 h after insulin administration by means of a jet injector, as well as statistically significant higher MBG values ($P < 0.05$), thus indicating a faster and shorter effect achieved in comparison to that produced by the syringe injected insulin.

Conclusions:

1. When switching the method of insulin administration in patients from needle syringe to jet injections the power of the jet injector should be increased (it can be set in three different levels). If that is not possible, because of patient skin characteristics then the dose of intermediary acting insulin should be slightly increased.
2. No local or general side-effects were registered using minimum injecting power of jet injector.
3. The results of the controlled poll have shown that this method of insulin administration is less painful and simpler for patients. The great majority of the patients would like to possess a jet injector.

Key-Words: *Type 2 Diabetes – Jet Injector – Needle Syringe – Free Insulin Profile – Blood Glucose Profile*

Introduction

In an effort to relieve pain and psychical stress accompanying insulin injections,other forms of insulin application in which the mentioned discomforts could be avoided or at least diminished, have been searched for. One attempt is the application of insulin by means of a jet injector using elevated pressure for insulin administration, i.e. without a needle. Although some authors (*Weller* and *Linder* 1966; *Cohn, Chez, Hingson, Szulman* and *Trimmer* 1972) have pointed to the similarity of pharmacokinetic characteristics of insulin applied by means of a jet injector and the classical injection route, recent studies (*Taylor, Home* and *Alberti* 1981; *Pehling* and *Gerich* 1984) argue for faster resorption and shorter action of insulin administered by means of a jet injector, which also leads to certain changes in the glycemia level.

The aims of this study were as follows: (1) To investigate the pharmacokinetic characteristics of a combination of fast- and intermediary-acting insulins in patients receiving one insulin dose daily (type 2) using the new generation jet injectors, which are much easier to handle with a very simple aspiration and pre-mixing of different types of insulin in an adequate ratio, and is considerably less expensive; (2) To study the possible local and general side-effects following the application of insulin by means of a jet injector (hematomas, necroses, scarrings); (3) To take a poll to obtain data on the simplicity and soreness due to the application of the device and on the patients' desire to possess it.

Materials and Methods

An informed consent was obtained from 20 diabetics (type 2) who took part in our study. The patients received a single dose of a combination of the fast- and intermediary-acting insulins in the morning. Details on age, sex, body weight, duration of diabetes, mean fasting and postprandial C-peptide values, usual insulin and dietary regimens are given in Table 1. On the first or second day (according to the plan of randomization) the usual insulin dose was applied with a jet injector or a needle syringe at 7.30 a.m. in the same skin area, i.e. in the abdominal wall. This was performed by the same physician educated in the procedure. The mean quantity of insulin administered to the patients during the study was 27.00±8.47 units (Actrapid MC, Monotard MC, NOVO), regardless of the method used. During the study, the patients were on a standard diet of constant energy intake with the meals being served at the same time each day. Blood samples were withdrawn at 12 time points (0, 10, 20, 40, 60 min, 2, 3, 6, 9, 12, 18 and 24 h) during 24 hours following the application of insulin. A new jet injector (SICIM, Romans d'Isonzo, Italy), belonging to the group of the spring-operated portable jet injectors, was used for the jet injection of insulin.

By pressing the button for releasing the spring, the desired amount of insulin penetrates through the skin. During the trial, the lowest possible injecting pressure was applied in all the patients, although choice could be quite easily made among the three optional injecting pressures (the device is provided with a pressure adapter). The instrument is capable of aspiring and mixing two types of insulin in the desired amounts, operating through a suitable selector valve.

The following measurements were carried out in the study: (1) Efficiency of a jet injector insulin application versus the subcutaneous needle syringe insulin application following glycemia (GOD-method) during the 24-h post-application period; (2) Resorption rate assessment by means of serum free, bound and total insulin

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Table 1 Characteristics of 20 type 2 diabetics studied.

Patient No.	Age (yr)	Sex	Ideal body weight (%)	Duration of diabetes (yr)	C-peptide fasting (nmol/l)	C-peptide postprandial (nmol/l)	Diet prescribed (KJ)	Total daily dose of insulin (U)
1	30	F	106.23	1	0.74	1.33	7550	26
2	59	F	119.84	6	1.00	2.01	6300	40
3	52	M	102.73	6	0.69	0.87	9240	36
4	24	F	105.18	1	0.56	0.61	5750	20
5	21	F	92.50	1	0.84	0.89	7550	16
6	35	M	109.51	7	0.71	0.94	6720	32
7	51	M	101.65	8	0.40	0.40	8400	32
8	30	F	110.77	2	0.66	0.63	6300	10
9	46	M	99.35	10	0.71	0.73	8000	12
10	57	M	107.83	5	0.37	1.01	6300	24
11	34	F	93.90	9	0.30	0.32	7950	32
12	61	M	103.98	14	0.63	1.18	7550	24
13	55	F	101.13	11	0.74	0.88	7100	36
14	44	M	97.63	1	0.52	0.85	8800	24
15	26	M	92.51	2	0.21	0.25	8800	36
16	52	M	76.24	2	0.45	0.96	7550	32
17	55	M	78.00	2	0.67	1.64	9660	36
18	25	M	97.84	0	0.35	0.87	8800	24
19	30	M	86.92	4	0.23	0.63	11300	20
20	51	M	108.07	30	0.58	0.62	6720	28
Mean	41.90		99.59	6.10	0.57	0.88	7817	27
±SD	13.47		10.75	6.88	0.21	0.42	1361.60	8.47

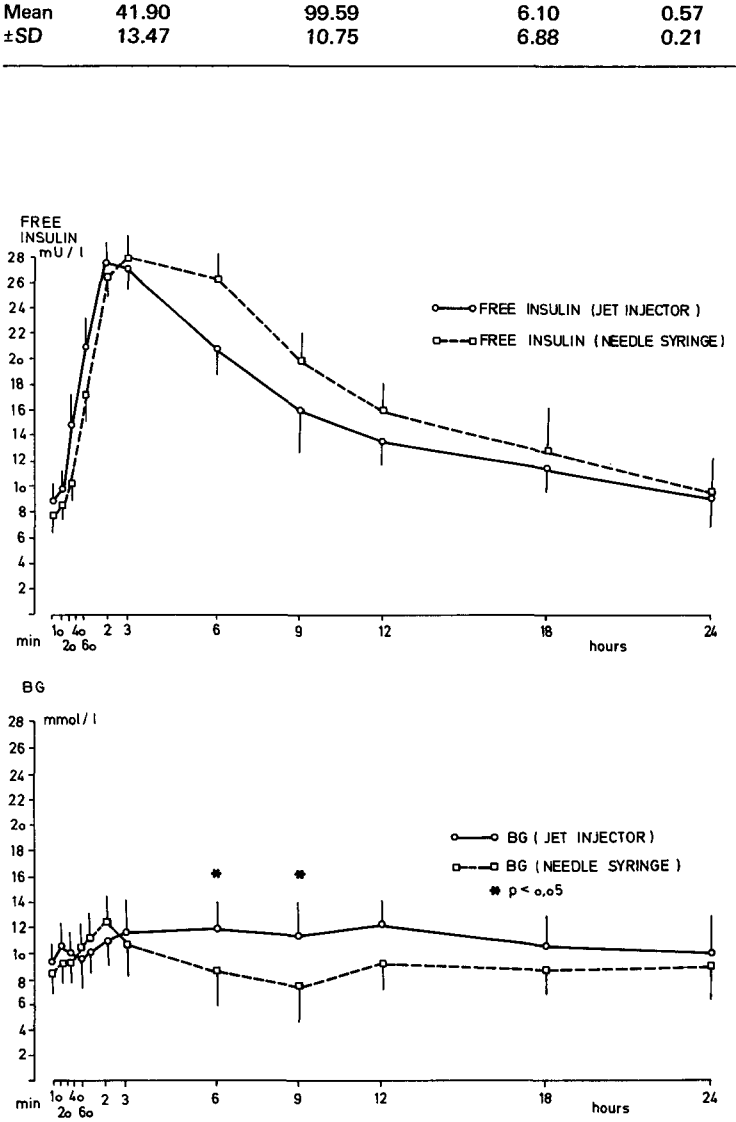

Fig. 1 Free insulin and blood glucose profiles after the insulin administration by means of needle syringe or a jet injector.

determinations, according to *Gennaro* and *Van Norman* 1975, using Phadeseph™ Insulin RIA kits, manufactured by Pharmacia Diagnostics AB, Uppsala, Sweden. When taking blood samples for analysis the insulin injection site was inspected and the patients were instructed to report any change to the physician (either local or general), possibly noted by themselves.

The data analysis was carried out using Student's paired t-test, whereas the results are expressed as mean±SD.

Besides this, a controlled poll was performed, consisting of answers to three questions posed to each patient:

1. Which kind of insulin application would be simpler and more practical in your daily life?
2. Which kind of insulin application is less painful?
3. Would you like to have a jet injector of your own?

Results

Fasting blood glucose and free insulin levels before the administration of insulin by means of needle syringe or jet injector were not significantly different on the two days (Fig. 1). Analyzing the serum free insulin profile after insulin application by means of a jet injector and after the usual needle syringe administration, no statistically significant differences between the methods were observed. A somewhat faster but not statistically significant increase in the free insulin level during the first hour, followed by lower free insulin levels in the period between 3 and 24 hours after the use of a jet injector, could be discerned (Fig. 1).

Overall mean blood glucose levels over the 24 h periods (MBG-Jet-Injector: 10.65±3.92 mmol/l; MBG-Needle Syringe: 9.94±3.0 mmol/l) were statistically significantly higher after the jet injection ($P < 0.05$). Analyzing the particular time points in blood glucose profiles, a statistically significant difference was found at 6 and 9 h after the insulin application only ($P < 0.05$).

The overall fluctuations of blood glucose (MAGE values) over the 24-h period by either of the methods, were not statistically significantly different (MAGE-Jet Injector: 6.13±4.25 mmol/l; MAGE-Needle Syringe: 6.28±2.29 mmol/l).

Analyzing the total and bound insulin levels, no statistically significant differences were observed at either of the time points.

No side-effects were observed in any of the patients after a jet injector insulin application using minimum injecting power.

The results of the controlled poll (Fig. 2) have shown the insulin application by means of a jet injector to be simpler for patients (16 patients preferred a jet injector), whereas 19 patients considered such application to be less painful in comparison to the usual needle syringe injection. A great majority of the patients would like to possess a jet injector (16 patients).

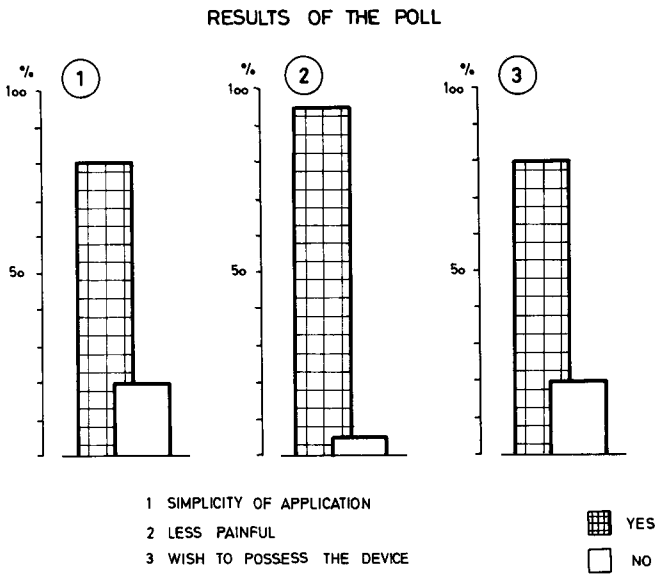

Fig. 2 Insulin administration by means of a jet injector.

Discussion

According to the results obtained in this study, a somewhat faster insulin resorption, followed by a lower free insulin level, could be discerned after the use of a jet injector, although no statistically significant differences were observed. This faster insulin resorption could be a consequence of insulin dispersion over a larger area, as small volume deposits of insulin are known to resorb at a faster rate (*Binder* 1969). Significant differences were observed in blood glucose profile, which appeared to match the slight modification in insulin kinetics. Insulin-glucose ratios could possibly enhance the significance of the changes in both parameters and reinforce the impression that insulin administered by a jet injector has a faster although shorter effect than that injected by means of a syringe. These results are similar to those obtained by others (*Taylor, Home* and *Alberti* 1981), although in this study a combination of fast- and intermediary-acting insulins was used in type 2 diabetics.

As the minimum possible power of the jet injector was used in this study for prevention of the possible local skin complications, the results have shown that the dose of intermediary-acting insulin should be slightly increased. The total dose and the dose of intermediary-acting insulin would remain the same, if the power of jet injector could be increased regarding the individual characteristics of the patient's skin (medium or maximum injecting power should be used). If the power of the jet injector or the dose of insulin should be increased, we can expect lower blood glucose values, as MBG values too.

Thus, it can be concluded that the application of insulin by the usual subcutaneous injections can be substituted by the use of jet injectors, which is less painful and simpler for the patient. No local or general side-effects were registered in the patients after the administration of insulin by means of jet injectors. However, the question of the possible local skin changes due to a long-term application of the device still remains to be elucidated.

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