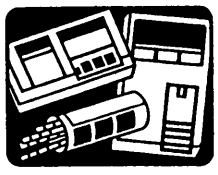
Technical Section



Development of New Jet Injector for Insulin Therapy

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To improve diabetic patients' compliance to multiple injection protocols, we developed and tested a new insulin jet injector, the Preci-Jet 50. The prototype has the following features: small size (14 × 2 cm) and weight (160 g), capability of mixing two types of insulin, accuracy and reliability of the ejected volume (dose), ease of use and sterilization, simplicity of design, and capacity of adjusting jet pressure to individual skin resistance. The ejected volume, evaluated by gravimetry, was more accurate and more reliable with the injectors (N = 18) than with 0.5-cc disposable plastic syringes (N = 18). The dead space of the injectors (N = 16), as evaluated by isotopic recuperation of radioactive insulin, was minimal, allowing mixed insulin injections. The human-device interface evaluation demonstrated that diabetic patients (N = 13) learned easily to manipulate the injector and that their ability to use it properly improved after 1 mo of use. We conclude that this injector may be a practical tool for insulin-dependent diabetic patients. DIABETES CARE 1986; 9:294–97.

Multiple insulin injections associated with self-monitoring of blood glucose remain the most accessible means to improve blood glucose control in insulin-dependent diabetes (IDDM).[1–6] However, pain or psychological aversion to needles sometimes decreases patients' compliance to multiple-injection protocols. An insulin jet injector may improve acceptability of such a regimen.

Jet injection was pioneered by Hingson and collaborators as early as 1947.[7–11] It consists of a high-pressure device that propels a fluid drug through a very fine orifice. At high velocity, the fluid pierces the epidermis and spreads into the subcutaneous tissues without the need to use a needle. Hingson and colleagues[7,10,11] and many other investigators[12–16] have used jet injection with success in the treatment of IDDM. It is our belief, however, that available devices are too cumbersome for the diabetic patient to carry around and that an improved, smaller injector would enhance the acceptability and utility of this method of insulin administration.

This article describes a new device and its functional modalities and briefly reports on the technical tests done to evaluate the accuracy of the ejected volume, the measurement of the dead space, and the level of human tolerance to the device. Later articles will report on clinical inpatient and outpatient trials.

DESCRIPTION OF THE DEVICE

The Preci-Jet 50 (Advanced Medical Technologies, Charlottetown, Prince Edward Island, Canada) has a cylindrical or pen shape. It weighs 160 g and measures 14 × 2 cm. It can be used to inject doses of 1–50 IU of U-100, 0.8–40 IU of U-80, or 0.4–20 IU of U-40 insulin.

Device parts. The main device components are (see Figure 1):

1) The power pack or handle contains the power source (springs), the clutch mechanism, and the trigger button. It is screwed inside the sleeve assembly.

2) The sleeve assembly contains the cylinder and the piston. Its distal head has a male threaded connector on which the nozzle or the vial holder (adaptor) can be adapted.

3) The nozzle contains the very fine orifice (diameter: 8/1000 in.) through which the fluid is ejected. It has a female threaded connector that is adapted on the head of the sleeve assembly.

4) The disposable vial holder contains a needlelike projection that is inserted into the insulin vial. One vial holder is placed on each insulin vial and left in place until the vial is empty.

Functioning. 1) Pressure is generated by screwing the handle clockwise inside the sleeve assembly. This compresses the

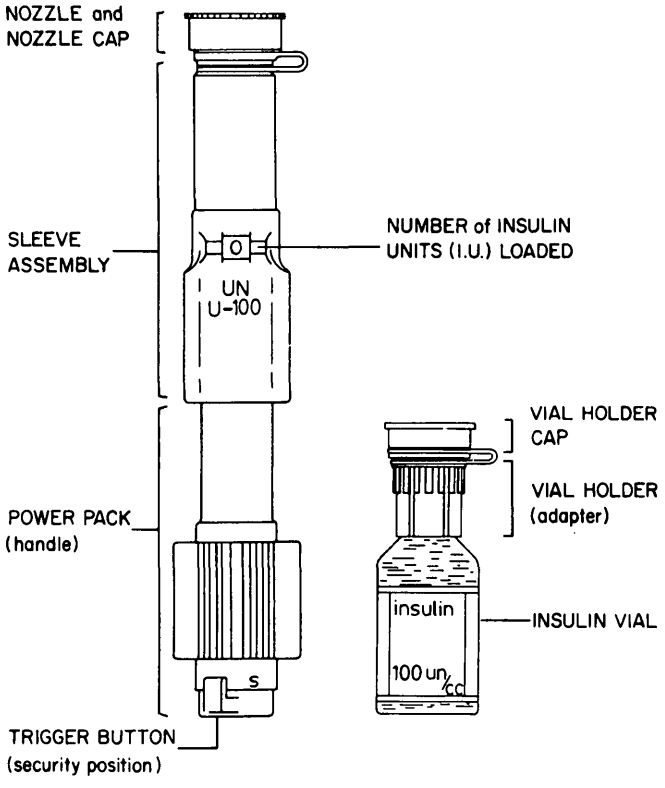

FIG. 1. Main components of the Preci-Jet 50 and the Adapt-o-Jet (vial holder). Injector is depicted in extended position as would be seen before pressure is applied. [A similar position is seen when injector is filled with maximum dose (50 IU insulin); under these conditions, "50" would appear in small glass window.]

springs inside the power pack. At the end of this movement, signaled by a click, a clutch mechanism holds the spring in the compressed position.

2) The nozzle is then unscrewed and replaced by the insulin vial, to which a vial holder has been attached previously (Figure 2). The vial holder perfectly matches the head of the sleeve assembly so that insulin flows directly into the cylinder. Thus, the dead space is virtually nil. The insulin enters into the cylinder through an orifice that is larger (diameter: 24/1000 in.) than the orifice of the nozzle, allowing a rapid flow without creating a vacuum. Furthermore, the former orifice never touches the skin, minimizing the risk of contamination.

3) The device is filled by turning the handle counterclockwise. This motion moves the piston back in a way similar to that of a regular syringe. As the device is filled, at each unit, the number of loaded units of insulin appears on a small window, and a click is heard and felt in such a way that a sightless patient can easily fill the device.

4) For a mixed-insulin injection, a second insulin vial, with its own vial holder, replaces the first one, and the same procedure is used until the desired total insulin dosage has been drawn up.

5) The nozzle is then put back in place.

6) Punch pressure adjustments can be made to adapt to individual skin resistance. For maximum pressure, no change is made, and one can proceed to step 7. At this setting, the distance between the spring (hammer) and the piston (nail) is maximum, and the injection triggers a strong hammering effect. To reduce the punch pressure to minimum, the handle is turned (clockwise) to a maximum five numbers back. By doing so, no insulin is released, but the distance between the hammer and the nail is reduced to zero, thus eliminating the hammering effect. "Backing off" to intermediate position (1–4) sets the device at intermediate punch pressures.

The proper "back off" for each patient can be found by practicing with saline injection. A fluid leak, or the appearance of a papule, indicates underpenetration of the injection

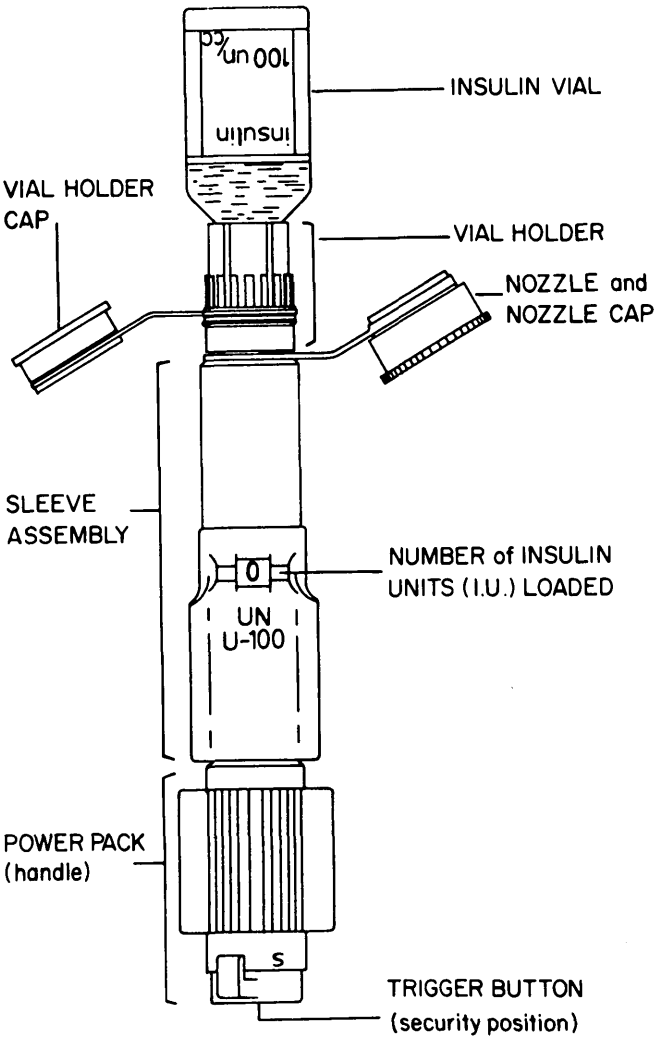

FIG. 2. Injector is ready to be filled with insulin. Pressure is generated by turning handle clockwise until a click is heard. Nozzle is unscrewed and replaced by vial holder and insulin vial. Injector is filled by turning handle counterclockwise until number on small window indicates the number of insulin units (IU) required. Then nozzle is screwed back into position.

TABLE 1
Human-device interface (N = 13): observation of injections done by patients

	Filling error (dosage)	Pressure adjustment	Device position	Injection stability	Pressure on skin		Sterility precautions
					During injection	After injection	
Tests done immediately after a 30-min instruction session (total: 78 injections)							
Number of errors	0	1	1	2	1	3	5
% of error	0	1%	1.3%	2.5%	1.3%	3.8%	6.4%
Tests done after 1 mo of outpatient use of the injector (total: 77 injections)							
Number of errors	0	0	1	0	0	0	2
% of error	0	0	1.3%	0	0	0	2.6%

and the need to increase punch pressure. Deep pain signifies excessive pressure, which should be reduced.

7) After disengaging the security button, the injector is held firmly and perpendicularly to the skin, the trigger is depressed with the thumb, and the insulin immediately flows into the skin.

8) Sterilization is recommended once every 3 wk in the following manner: disassemble the device by removing the nozzle, nozzle cap, sleeve assembly, and power pack. The first three parts are placed in boiling, demineralized water for 20 min; after drying, they are reassembled.

TECHNICAL EVALUATION

Precision tests. The accuracy and reliability of the ejected volume were evaluated by gravimetry. The following standard volumes were studied: 5, 10, 20, 30, 40, and 50 units of insulin volume equivalents (IU). The results (in terms of errors observed minus standard volume deviates) with 18 jet injectors were compared with those with 18 0.5-cm^3 disposable plastic syringes (Plastipak, Becton-Dickinson, Mississauga, Ontario, Canada). An analysis of variance was used to test the type of device effect (injector versus syringe), the standard volume effect (comparison of the six volumes), the order effect, and various interactions between these factors.

The errors were -0.24 ± 0.65 IU (mean $\pm$ SD) for the injectors as compared with -1.45 ± 1.01 IU for the syringes ($P < .001$). The relative error means were 0.95 and 5.61% for the injectors and the syringes, respectively. Thus, the jet injectors were more accurate (mean) and more reliable (SD) than the syringes. However, these errors are unlikely to have any clinical significance for both devices, representing a bias of $+0.20$ to -0.59 IU (injectors) and of -0.20 to $+2.88$ IU (syringes) for insulin doses varying from 5 to 50 IU of insulin.

Dead-space measurements. For mixed-insulin injections, the dead space of the injectors must be minimal; otherwise, the residue from a first injection would contaminate the following one and change the proportion of each type of insulin. The dead space was measured on 16 injectors by isotopic recuperation in unlabeled insulin injections following a radioactive insulin injection. The estimated volume of residual insulin was 0.0013 cm^3 (0.13 IU of insulin) to 0.0055 cm^3 (0.55 IU of insulin) for doses of 5–50 IU insulin. Such a minimal residue cannot significantly alter the following injection.

Human-device interface evaluation. This jet injector is designed to be used at home by patients. To assess the human factors that can influence its use, 13 insulin-dependent diabetic patients (age 26 $\pm$ 3 yr) attended a 30-min instruction session on the use of the injector. After the session, using two bottles of saline solution, they injected themselves six times with the same volumes they were accustomed to using on a regular basis. Throughout these six injections, they were observed for *1*) ability to fill the injector with accurate volume, *2*) ability to adjust the back-off pressure, 3) ability to inject themselves properly, and 4) ability to avoid device contamination.

The evaluation done immediately after teaching the technique revealed 13 (16.7%) errors for 78 injections (Table 1). After having used the device at home for 1 mo, the same patients underwent a second evaluation. The number of errors decreased to 3 (3.9%) for 77 injections. Note that most of the errors represent minor deviations from the recommended technique and would neither diminish the accuracy of the injection nor produce contamination of the vials. Furthermore, most of the sterility errors cannot occur with the modified prototypes. (The errors consisted of putting the wrong side of the nozzle on the table. The new prototype nozzles will remain attached to the sleeve assembly.) Note that no dosage (filling) error occurred, even in the first evaluation. Thus, this evaluation showed that the use of the injector is relatively easy to learn.

DISCUSSION

Jet injectors may improve patient compliance to a regimen of multiple insulin injections. In this article, we describe a jet injector prototype that was designed specifically for daily use by insulin-dependent diabetic patients. Its small size (14 $\times$ 2 cm) and weight (160 g) and its practical format allow the patient to carry it easily during daily activities. The punch pressure is adjustable and

can be adapted to the patient's skin resistance. The jet injector is accurate and reliable. It can be used for mixed-insulin injection. It is easy to manipulate and to sterilize and can be used by sightless patients. In conclusion, this jet injector could prove to be a practical tool for diabetic patients.

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REFERENCES

[1] Sonksen, P. H., Judd, S. L., and Lowy, C.: Home monitoring of blood glucose. Method for improving diabetic control. Lancet 1978; 1:729–32.

[2] Walford, S., Gale, E. A., Allison, S. P., and Tattersall, R. B.: Self monitoring of blood glucose. Improvement of diabetic control. Lancet 1978; 1:732–35.

[3] Skyler, J. S., Lasky, I. A., Skyler, D. L., Robertson, E. G., and Mintz, D. H.: Home blood glucose monitoring as an aid in diabetes management. Diabetes Care 1978; 1:150–57.

[4] Irsigler, K., and Bali-Taubauld, C.: Self-monitored blood glucose: the essential biofeedback signal in the diabetic patient's effort to achieve normoglycemia. Diabetes Care 1980; 3:163–70.

[5] Schiffrin, A., and Belmonte, M.: The importance of frequent self glucose monitoring with continuous subcutaneous insulin infusion (CSII) and multiple subcutaneous injections (MSI). Diabetes 1982; 31:255–64.

[6] Skyler, J. S., Skyler, D. L., Seigler, D. E., and O'Sullivan, M. J.: Algorithms for adjustment of insulin dosage by patients who monitor blood glucose. Diabetes Care 1981; 4:311–18.

[7] Hingson, R. A., and Hughes, J. G.: Clinical studies with jet injection: new method of drug administration. Anesth. Analg. 1947; 26:221–30.

[8] Hingson, R. A.: Development of the hypospray for parenteral therapy by jet injection. Anesthesiology 1949; 10:65–75.

[9] Hingson, R. A., and Figge, F. H.: Survey of development of jet injection in parenteral therapy. Anesth. Analg. 1952; 31:361–66.

[10] Cohn, M. L., Chez, R. A., Hingson, R. A., Szulman, A. E., and Trimmer, M.: Use of jet insulin injector in diabetes mellitus therapy. Diabetes 1972; 21:39–44.

[11] Cohn, M. L., Hingson, R. A., Narduzzi, J. V., and Seldon, J. M.: Clinical experience with jet insulin injection in diabetes mellitus therapy: a clue to the pathogenesis of lipodystrophy. Ala. J. Med. Sci. 1974; 11:265–72.

[12] Grüneklee, D., Meyer, M., and Ruppert, C.: Subcutaneous administration of insulin by a variable dose jet injector. Abstract. Diabetologia 1978; 15:236.

[13] Perkin, F. S., Todd, G. M., Brown, T. M., and Abbott, H. L.: Jet injection of insulin in treatment of diabetes mellitus. Proc. Am. Assoc. 1950; 10:185–99.

[14] Perkin, F. S.: Jet hypodermic injectors for use in diabetes (letter). J. Am. Med. Assoc. 1966; 7:206.

[15] Weller, O., and Linder, M.: Jet injection of insulin versus the syringe and needle method. J. Am. Med. Assoc. 1966; 195:844–47.

[16] Chiasson, J. L., Ducros, F., Poliquin-Hamet, M., Lopez, D., Lecavalier, L., and Hamet, P.: Continuous subcutaneous insulin infusion (Mill-Hill Infuser) versus multiple injections (Medi-Jector) in the treatment of insulin-dependent diabetus mellitus and the effect of metabolic control on microangiopathy. Diabetes Care 1984; 7:331–37.