

# Insulin pens dribble from the tip of the needle after injection

M. Annersten, A. Frid\*

## ABSTRACT

**Aim.** To study different insulin pens regarding leakage from the tip of the needle after injection.

**Patients and method.** Six pens were tested; Saline Pen 3.0 ml (Lilly), B-D Pen 3.0 ml, NovoLet 1.5 and 3.0 ml, NovoPen 1.5 and 3.0 ml. Twenty volunteers were injected with sterile saline and the needle was withdrawn after 1, 3, 5, or 7 s respectively. Any dribble was collected on a filter paper and weighed. The procedure was videotaped.

**Results.** There was a minimum of dribbling from the 1.5 ml pens. Eight out of 20 NovoPen 3.0 ml and B-D Pen 3.0 ml, 16 out of 20 NovoLet 3.0 ml, and 19 out of 20 Saline Pen (Lilly) dribbled after a 7 s hold-in time. The 8 B-D Pen 3.0 ml had leaked 4.0 mg (2.4–18.8), the 8 NovoPen 3.0 ml 4.7 mg (3.8–6.7), the 16 NovoLet 3.0 ml 5.0 mg (3.1–16.6) and the 19 Saline Pen 3.0 ml had leaked 9.2 mg (4.9–19.1).

**Conclusion.** There is a clinically significant leakage of fluid from the needle tip even after 7 s hold-in time. Patients should be taught to hold the needle in for at least 10 s to be assured they get the intended dose. Copyright © 2000 John Wiley & Sons, Ltd.

Practical Diabetes Int 2000; 17(4); 109–111

## KEY WORDS

diabetes; insulin injection; insulin pen; insulin wastage; insulin leakage; needles; air bubbles

## Introduction

Injection pens for insulin treatment have been available on the market since they were introduced by Novo Nordisk (formerly Novo) in 1985. In many countries more than 90% of diabetic patients who require insulin use the insulin pen. A modern insulin regimen consists of a meal bolus injection combined with basal insulin, usually at bedtime. Insulin is thus delivered several times daily and accuracy and consistency of the

delivered dose is of great importance. Patients have observed that insulin may leak from the tip of the needle several seconds after the injection is completed. This problem has most often been attributed to air bubbles in the cartridges.<sup>1,2</sup>

When injecting with an 'ordinary' insulin syringe, the pressure on the rubber plunger ceases when the injection is finished. If the plunger has become compressed it can move backwards when the pressure has ceased. The liquid will therefore not continue to be pressed through the needle.

When injecting with an insulin pen, there is a locking mechanism making the piston unable to move backwards. Any pressure that has been accumulated in the system is able only to be equalized by the liquid being pressed through the needle. Thus at a fast injection, liquid may continue to be pressed through the needle long after the pressure on the piston has ceased. The problem may be augmen-

ted by the narrow gauge of modern injection needles. To minimize the problem, it is important that there are no air bubbles inside the vial, as air, opposed to liquid, is compressible. In this study we found air in six (out of 120) pens or cartridges prefilled with saline fluid, in contrast to Ginsberg *et al.*<sup>1</sup> who found air in 42 out of 50 insulin cartridges. In our study the air was removed by a procedure described in the Patients and Methods section. This procedure, described by Hanas 1998,<sup>3</sup> differs from advice given by all manufacturers of insulin pens and cartridges.<sup>4–8</sup> The manufacturers advice patients to remove air with the needle already attached to the pen. Since the 'cartridge end' of the needles protrudes 2 mm below the rubber membrane the air will be trapped above the tip of the needle allowing liquid to flow through the needle with air still present in the cartridge. The procedures suggested by the manufacturers probably increase insulin loss

M. Annersten, RN, Bachelor of Nursing,  
A. Frid, MD, PhD, Department of Internal  
Medicine/Diabetes and Endocrinology,  
University Hospital of Lund, Sweden

\*Correspondence to:

Dr A. Frid  
Department of Internal Medicine/Diabetes  
and Endocrinology University Hospital of  
Lund, S-221 85 Lund, Sweden.

Submitted: 30 April 1999

Accepted in revised form: 1 November 1999

## Insulin pen dribble

without solving the problem of air bubbles in the cartridge.

**Aim**

To study different insulin pens regarding leakage from the tip of the needle after varying hold-in times after injection.

**Patients and method**

Twenty volunteers participated. Ten were women. Median age was 33 years (20–49). Median body mass index was 23.0 (19.2–36.0) kg/m<sup>2</sup>.

Six insulin pens were studied: NovoLet (PenSet) 1.5 ml, NovoLet (PenSet) 3.0 ml, NovoPen 1.5 ml, NovoPen 3.0 ml, (Novo Nordisk A/S, Bagsvaerd, Denmark) Saline Pen 3.0 ml (Lilly France S.A. Fegersheim, France), and BD-pen 3.0 ml (Becton-Dickinson Europe Meylan Cédex, France).

NovoFine 0.30 × 8 mm needles (Novo Nordisk Pharma A/S, Bagsvaerd, Denmark) were used for their respective pen, and MicroFine 0.25 × 8 mm needles (Becton Dickinson, Franklin Lakes, NJ, USA) were used for the Lilly and BD-pen.

In six cartridges air was removed by the following procedure. Holding the pen without needle in a vertical position 2 IU are dialled and the button pressed to the bottom. The cartridge is gently tapped to allow the air to collect under the then slightly bulging rubber membrane. When the needle slowly penetrates the rubber membrane the air escapes. If fluid did not appear the procedure was repeated.

All injections were performed by the same investigator (M.A.) and the injection time was 2 s, measured with a timer (Dual Digital Timer, Oregon Scientific, Portland, OR, USA) held by the investigator. The volunteer pinched a skinfold in the abdominal area with one hand, and with the other hand he held a filter paper for the drops to fall on. The investigator injected 0.2 ml of sterile saline. The needle was then withdrawn after 1, 3, 5 or 7 s respectively. If there was any dribble at 1 s, the experiment went on

to 3 s, and further on until no dribble was noticed or 7 s hold-in time was reached. If there were no dribble after 1 s, the test with that pen was interrupted. The maximum number of injections were 24 (six pens at 1, 3, 5 and 7 s) which was considered the highest feasible number of injections for one volunteer in one session.

The liquid was collected on the filter paper and weighed on a Precisa 290 Balance (Precisa Instruments AG, Dietikon, Switzerland) measuring four decimals to the gram. The result was immediately read and written in the protocol, avoiding evaporation. The whole procedure was documented on videotape by a Panasonic Video Camera NV-DS77EG (Matsushita Electronic Industrial Co., Ltd, Osaka, Japan).

The study was approved by the local ethical committee.

**Results**

There was no leakage from NovoPen 1.5 ml and NovoLet 1.5 ml after 7 s. One NovoPen 1.5 ml and one NovoLet 1.5 ml leaked after 5 s. After 3 and 1 s two NovoLet 1.5 ml leaked. Eight out of 20 NovoPen 3.0 ml and BD-pen 3.0 ml, 16 out of 20 NovoLet 3.0 ml and 19 out of 20 Saline Pen (Lilly) dribbled after a 7 s hold-in time (see Table 1).

After a 7 s hold-in time, the 8 B-D Pen 3.0 ml had leaked 4.0 mg (2.4–18.8), the 8 NovoPen 3.0 ml 4.7 mg (3.8–6.7), the 16 NovoLet 3.0 ml 5.0 mg (3.1–16.6) and the 19 Saline Pen 3.0 ml had leaked 9.2 mg (4.9–19.1) (see Table 2).

One International Unit of Insulin is roughly estimated to 0.01 mg saline

fluid. Thus the estimated median loss of insulin after 7 s amounts to 0.40 IU for the 8 dribbling B-D Pen 3.0, 0.47 IU for the 8 NovoPen 3.0, 0.50 IU for the 16 NovoLet 3.0, and 0.92 IU for the 19 Saline Pen.

**Drop outs**

In one case, the investigator partly missed the paper and some drops were lost. In two cases blood was mixed with the fluid and the result excluded.

**Discussion**

Considering the great number of 3 ml insulin pens leaking even after 7 s, we should recommend the patients to keep a hold-in-time for at least 10 s. This seems to be the case especially when using the Lilly 3.0 ml pen.

It is essential that patients can have confidence in their injection devices and the written information accompanying them and that they can be sure that they receive the intended dose of insulin at every occasion. The teaching on injection technique should be carried out according to studies regarding this matter.

Advice about hold-in-time has earlier mostly considered the risk of insulin leaking from the skin or blood being drawn into the cartridge. The risk of dribbling from the needle has not been a major issue.

Lilly recommend in the Swedish information pamphlet from 1999<sup>4</sup> a 5 s hold-in-time. In this study this seems to be insufficient. Novo Nordisk recommend in their leaflet for NovoPen<sup>5</sup> a 6 s hold-in-time, the same recommendation follows the vials for NovoLet. This recommendation seems not to be sufficient for the

Table 1. Number of dribbling insulin pens after 4 different hold-in times

	7 s	5 s	3 s	1 s
NovoLet 1.5	0	1	2	2
NovoLet 3.0	16	17	19	18
NovoPen 1.5	0	1	4	11
NovoPen 3.0	8	11	17	20
Saline Pen 3.0	19	19	19	20
BD-pen 3.0	8	13	16	18

## Insulin pen dribble

Table 2. Median weight in mg (range) of the fluid from the leaking insulin pens

	7 s	5 s	3 s	1 s
NovoLet 1.5	0	3.8	3.3 (3.3–3.9)	4.6
NovoLet 3.0	5.0 (3.1–16.6)	6.6 (2.6–11.7)	9.2 (3.1–16.0)	8.9 (3.0–18.2)
NovoPen 1.5	0	3.5	3.6 (3.4–6.3)	4.7 (3.0–7.2)
NovoPen 3.0	4.7 (3.8–6.7)	4.4 (3.0–7.5)	5.4 (2.8–8.3)	6.2 (2.1–9.4)
Saline Pen 3.0	9.2 (4.9–19.1)	10.3 (5.0–14.6)	11.8 (5.3–23.7)	16.8 (2.8–29.7)
BD-pen 3.0	4.0 (2.4–18.8)	4.7 (2.0–8.9)	5.0 (3.0–24.0)	6.9 (2.9–15.4)

3 ml pen. BD do not mention hold-in-time in their information leaflet.<sup>6</sup>

It seems that the information material regarding this matter need to be updated.

Since the purpose with an injection is to give the patient a certain amount of insulin attention must be paid to the possibility of insulin loss due to short hold-in time. This also seems to be affected by the design of the insulin pen.

Some further points regarding insulin loss is worth mentioning.

BD recommends<sup>6</sup> the discharge of 4 IU in the air and thereafter 2 IU until a drop of insulin is seen at the tip of the needle.

Lilly recommend<sup>4</sup> to discharge 2 IU in the air at each needle shift which in practice means before every injection.

In the information brochure attached to the NovoPen 3.0 ml<sup>8</sup> it is also recommended that 2 IU are purged before every injection.

Recommendations regarding needle replacement are closely related to

insulin loss and air bubbles. Novo Nordisk recommend to remove the needle after each injection *to avoid liquid to leak*.<sup>5</sup> Lilly recommends the same procedure when using the 3.0 ml pen, but their explanation is *to avoid air entering the vial*<sup>4</sup> or *to avoid needle blockage and to keep sterility*.<sup>7</sup> BD again gives the same advice but the explanation is *maximum injection safety and comfort*.<sup>6</sup>

If the patient receives different amounts of insulin each time depending on hold-in-time and air bubbles in the cartridge, this might lead to unstable blood glucose levels. A patient regularly experiencing leakage, may increase the dose of insulin. If then the patient keeps a longer hold-in-time, there is a risk of hypoglycemia. This problem may be more important for children and insulin sensitive patients with multi injection treatment.

The demands on the pens increase all the time, as they become more and more commonly used. They have to

be reliable, they must tolerate rough handling as the patients constantly brings them with them. Finally they must be easy to handle for the visually or physically impaired patient.

In the future it must be studied how patients inject insulin in the everyday life and find out how to improve teaching.

## References

- Ginsberg BH, Parkes JL, Sparacino C. The Kinetics of Insulin Administration by Insulin Pens. *Horm metab Res* 1994; **26**: 584–587.
- Chantelau E, Heinemann L, Ross D. Air bubbles in insulin pens [letter]. *Lancet* 1989; **8659**: 387–388.
- Hanas R. *Insulin-Dependent Diabetes in Children, Adolescents and Adults*. Lund; Piara, 1998; 99.
- Eli Lilly Sweden AB. *How to Use Your Pre Filled Insulin Pen from Lilly*, information pamphlet (Swedish version). Stockholm: Lilly; 1999.
- Novo Nordisk A/S Bagsvaerd. Leaflet from the Novolet package (Swedish version). 1997.
- Becton Dickinson Stockholm. *Users Instruction Following the BD-Pen* (Swedish version). 199.
- Leaflet from Lilly Humalog Pen package (Swedish version). 1997.
- Novo Nordisk A/S Bagsvaerd. *Users Instruction Following the NovoPen 3.0 ml* (Swedish version). 1996.

## WEBSITE NEWS

John Wiley & Sons will soon be launching a Website dedicated to diabetes. This will contain areas of interest to all members of the diabetes community: research scientists, clinicians, representatives of the pharmaceutical industry and patients.

### Features of the site will include:

- The full content of *Practical Diabetes International*, and articles from the journal *Diabetes/Metabolism Research and Reviews*
- Material from selected Wiley books on diabetes, including the *International Textbook of Diabetes Mellitus* (Second Edition) edited by K.G.M.M. Alberti, and the two British Diabetic Association guides *Living with Diabetes*
- A news section providing up-to-date information from the pharmaceutical industry
- A directory of drugs and devices available to diabetic patients and their clinicians, with basic information on all products and in-depth dossiers on selected products
- A continuing education section for health-care practitioners at all levels
- A Directory of Diabetes-related training courses in the UK

A feedback service will provide a valuable opportunity for the different members of the diabetes community to interact, improving their ability to work together towards a common goal – a better quality of life for diabetic patients.