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Insulin delivery using pen devices

Simple-to-use tools may help young and old alike

Nancy J. V. Bohannon, MD

PREVIEW

Clinical trials have convincingly demonstrated that improved glycemic control significantly reduces the risk of diabetes-related complications. However, tight control is not always easy for patients to achieve. To help overcome some of the problems linked with tight control, insulin pen devices have been developed to offer easier, safer, more accurate, and more discreet insulin injection. In this article, Dr Bohannon provides information about these insulin pens and discusses which patients are most likely to benefit.

With the rapid pace of modern life, the time required to optimally manage diabetes may be hard to find. New insulin and insulin delivery systems can make this easier while offering additional benefits of lifestyle flexibility and improved glycemic control. Insulin analogues, such as insulin lispro (Humalog), also improve convenience by their rapid action; this allows insulin injection immediately before meals, rather than the 30- to 60-minute interval needed for the best postprandial glucose control with regular insulin.

Insulin pens are another innovation designed to provide the patient with an easy-to-use, convenient, and accurate method of insulin delivery. The goal is to improve glycemic control by making it less difficult to follow the current recommendations for intensive insulin regimens.

Two types of insulin pens are available today: prefilled and reusable. Prefilled pens are simply discarded when the insulin cartridge is spent, whereas reusable pens contain a replaceable insulin cartridge that is loaded into and removed from the pen by the patient. Most pens function on simple mechanical principles and are durable. The technique for insulin delivery is similar for both prefilled and reusable pens.

Technical advances

Medical therapy for diabetes mellitus has changed dramatically since Banting and Best discovered insulin in 1921. Not only have therapies for diabetes advanced significantly, but the technology for the delivery of insulin has also changed. Nonetheless, syringes were the sole method of insulin delivery for decades. The original glass syringes and their large, reusable needles had to be boiled for sterilization. The needles were sharpened with a pumice stone for reuse. Syringes continue to play a prominent role in patient care today, but they are now disposable plastic devices that deliver as little as 0.5-unit dosing increments through 30-gauge, short, attached needles.

Although advancements in technology have provided various sizes of syringes and needle systems, the traditional insulin injection process remains time-consuming, cumbersome, inconvenient, and somewhat painful. Furthermore, insulin dosing via syringe is associated with a high risk of dosage errors; as many as 80% of patients carry out some aspect of insulin administration via syringe incorrectly.[1] Now, to allow more flexibility and convenience, patients are seeking options other than the traditional vial-and-syringe delivery method. Insulin pens meet this need and also address issues of patient and environmental safety, social concerns, and more accurate dosage control (table 1).

Insulin pen devices are unique

continued

Table 1. Advantages of insulin pen devices over conventional insulin syringes

- More convenient insulin delivery
- More accurate dosing
- Less pain because smaller-gauge needles are used
- Better quality of life
- Easier compliance with insulin regimen
- Simpler for specific populations to use (eg, older adults, children and adolescents, pregnant women)
- Improved social acceptability, especially at school
- More flexibility because of disposable or reusable options

in that they combine the insulin container and the syringe in a single unit. Their compact size allows discreet insulin administration but still provides extremely accurate insulin delivery. Advances in the technology of needle manufacturing continue to make needles more comfortable to use.[2] With all these refinements combined, insulin pens improve the likelihood that patients will adhere more closely to recommended insulin dosing schedules.

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Pen types and styles

Insulin pens have become extremely popular throughout the world; in some countries, 70% to 90% of all insulin is delivered by pen.[3] However, in the United States only about 2% of insulin is injected via pen. This is probably because of difficulties with reimbursement from insurance companies or a lack of knowledge on the part of patients and physicians about pen availability. The fact is that insulin pens are available in various types and styles (table 2) and can benefit a large number of patients.

Prefilled pens

Prefilled pens contain a built-in, single-use insulin cartridge. Because this device requires no loading by the patient, it is especially convenient and easy to use. These portable, durable, and lightweight delivery systems are particularly helpful for patients who have difficulty handling the cartridges in reusable pens or people with busy schedules who prefer not to have to stop to change cartridges. However, prefilled pens may be slightly more expensive over time, compared with reusable pens. Also, both types of pens are more expensive than vial-and-syringe insulin therapy.

In the United States, the first prefilled pen was the Novolin 70/30, introduced in 1993; the newest prefilled pens are the insulin lispro (Humalog) and human insulin (Humulin) devices manufactured by Eli Lilly & Company. These pens have single-unit dosing increments, audible clicks when dialing the dose, a large magnifying window that shows unit dose, two-way dose setting that allows the user to decrease the dose without taking the pen apart or discharging insulin from the pen, and an end-of-dose click that indicates that the full dose has been delivered.

Reusable pens

With the reusable pen, the patient inserts an insulin cartridge into the pen's delivery chamber. For some patients, this allows greater flexibility (ie, changing types of insulin without needing to buy another pen if prescription changes), and it may be more economical than using prefilled pens. In addition to being durable and easy to use, the reusable pens are designed for longer duration of use. Disadvantages of the reusable pens are the potential loss of sterility with use[4,5] and the possible damage that may occur to the pen over time.

With individual use of the pen device, the risk of infection is minimized.[5] Among the reusable pens currently on the US market are: Autopen AN 3000 and AN 3100 (Owen Mumford, Inc.),

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B-D Pen Classic and B-D Pen Mini (Becton Dickinson), NovoPen 1.5 and NovoPen 3.0 (Novo Nordisk), and Humalog and Humulin pens (Lilly).

Device preparation

Regardless of whether a patient chooses the prefilled or the reusable pen design, the techniques for dose preparation and insulin delivery are generally similar. Once a disposable needle is screwed on to the pen and the pen is primed, the patient simply dials to the appropriate dose, which can be seen in the device's display window and can be heard as audible clicks in many pen devices. The needle is inserted subcutaneously, and the plunger injection button is depressed to deliver the dose. One disadvantage of pen devices is that the injection itself takes slightly longer than does the traditional syringe injection. The pen needle should remain in the subcutaneous tissue for 5 seconds after complete depression of the plunger.

Insulin cartridges are available in either a 1.5-mL or 3.0-mL volume (150 U or 300 U, respectively) and are specific for the pen size (ie, a 150-U cartridge will not fit in a 300-U pen, and vice versa).

The following insulins are currently available in 1.5 mL cartridges: regular human insulin (Humulin R, Novolin R), human isophane insulin suspension (Humulin N, Novolin N), 70% human isophane insulin suspension with 30% regular human insulin (Humulin 70/30, Novolin 70/30), and insulin lispro (Humalog).

Insulin pen devices are unique in that they combine the insulin container and the syringe in a single unit.

The cartridges should be stored in the refrigerator before use. However, once a cartridge is placed in a reusable pen, the pen can be kept at room temperature (<86°F) for a month, as long as it is away from direct heat and light.

The pen and cartridge configurations vary, so that only Lilly 3.0-mL cartridges fit Lilly, Becton Dickinson, and Owen Mumford 3.0-mL pens. Novo Nordisk 3.0-mL cartridges fit only 3.0-mL NovoPens. The Disetronic pens accept any insulin but require use of Disetronic cartridges.

The disposable needles that are attached to insulin pens have some advantages over standard syringe needles. Manufacturers offer pen needles that are one third shorter (12.7 mm) than standard-length needles and are a larger gauge (thus a smaller bore diameter) for greater patient comfort. Because the pen needle does not puncture the stopper of an insulin vial before injection, the needle maintains its sharpness and beveled angle, thereby potentially reducing the pain of injection, compared with the traditional vial-and-syringe technique.

Clinical studies

Although insulin pens have been available for more than a decade, few clinical studies in the United States have evaluated their use. After the pen's introduction in 1985, Jefferson and associates[6] evaluated patient preferences and blood-glucose control indexes in 10 adolescents with diabetes, aged 12 to 17 years. Over a 3-month period, mean glycosylated hemoglobin (HbA_{1c}) levels decreased from 13.7 ± 2.7% to 11.7 ± 3.4%. Most patients, including those who had increased their injections from once daily to four times a day, reported the pen's advantages outweighed the inconvenience of multiple injections. One of the first pen devices on the market was used in this study. Since that time, pens have undergone many significant improvements.

In 1993, Plevin and Sadur[7] assessed the acceptance of pen injections among 64 adult patients—19 with type 1 and 45 with type 2 diabetes. Most of the patients had been treated with insulin for 6 months to 43 years before the study; 22 of the 64

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patients were new insulin users.

During the 4-week study, mean fasting blood glucose concentration decreased from 197 mg/dL to 171 mg/dL ($P<.05$), and none of the patients reported an episode of moderate or severe hypoglycemia. Patient comments regarding the pen were extremely positive: 98% reported the pen was convenient and easy to use, and 91% wanted to continue its use.

In an Italian study,[1] the safety, efficacy, and acceptability of a prefilled insulin injection pen device was assessed in 60 patients with diabetes who were over 50 years of age and were using conventional insulin syringes. Hypoglycemic episodes did not differ significantly among patients using syringes compared with those using pens, and no marked hypoglycemia was noted. Blood glucose profiles were similar for both types of insulin administration, except for prelunch blood glucose values, which were lower with pen use (157 ± 52 mg/dL versus 166 ± 49 mg/dL [$P<.01$]). About 90% of patients administered insulin more quickly and easily with the pen than with the conventional syringe.

The investigators concluded that the prefilled insulin pen was safe, efficacious, and highly accepted in patients with diabetes over age 50.[1] Ease of accurate dosing is particularly important for older patients, who may have impaired vision, arthritis, or

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Table 2. Features of commercially available insulin pen devices

	B-D Pen Classic 1.5 mL (Becton Dickinson)	B-D Pen Mini (Becton Dickinson)
Physical characteristics		
Prefilled	N	N
Reusable	Y	Y
1.5 mL, 150 units	Y	Y
3.0 mL, 300 units	N	N
3.15 mL, 315 units	N	N
Pediatric "POP" pens	Y	Y
Special color graphics	Y	N
Viewed size of dose numbers greater than or equal to 0.1 in. (or clip-on magnifier)	N	N
Dosing features		
Manufacturer's stated dosing increment (units)	1	0.5
Minimum/maximum dose (units)	1/30	0.5/15
Dark dosing number on light background	Y	Y
Dial and dose using same knob	Y	Y
Two-way dose dialing	N	N
Audible click when dialing	Y	Y
Audible click when injecting	Y	Y
End of injection stroke indication	Y	Y
Insufficient remaining dose (predose indication)	N	N
Indicator returns to zero at dose completion	Y	Y

N, no; NPH, isophane insulin suspension; R, regular insulin; Y, yes.

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