

Insulin Devices

Addressing Barriers to Insulin Therapy With the Ideal Pen

Purpose

The purpose of this article was to identify and address barriers to initiating insulin therapy in patients with type 2 diabetes.

Results

Insulin pen devices address many of the mechanical barriers associated with a syringe and vial. In addition, pen devices are increasingly being improved, offering long-term pen users benefits over earlier pen users. These devices can be tailored to address the specific needs of different patient populations, such as elderly patients or those with visual or manual dexterity disabilities. Although insulin devices offer benefits over the syringe and vial, features desirable in the ideal pen have not been established.

Conclusions

Data suggest that currently available insulin pens possess various features that make them suitable for particular patients. Individual needs of each patient should be considered before an insulin pen device is prescribed.

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For patients with type 1 or type 2 diabetes, achieving and maintaining tight glycemic control is paramount for reducing the risk of developing long-term complications.^{1,2} It is increasingly apparent that patients with type 2

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diabetes benefit from early addition of insulin to oral antidiabetic agents in their therapeutic regimen.^{3,4} However, numerous barriers prevent or delay the initiation of insulin. This article identifies key barriers to insulin administration and discusses the use of several insulin pen devices.

Barriers Associated With Insulin Administration

Fear of weight gain and hypoglycemia are 2 key factors that prevent or delay the initiation of insulin therapy in patients with type 2 diabetes.^{5,6} The introduction of insulin analogs, such as insulin glargine⁷ and insulin detemir,⁸ has lessened the risk of hypoglycemia and limit weight gain versus traditional insulins, such as neutral protamine Hagedorn (NPH) insulin.

Also, a number of barriers to initiating insulin therapy are not caused by insulin therapy. The method by which insulin is administered has been shown to affect patient acceptability of insulin therapy and quality of life and may serve as a key barrier to the initiation of insulin.⁹ The traditional way to administer insulin—using a syringe and vial—is associated with several disadvantages, making it unpopular and unsuitable for many patients with diabetes. Visual impairment and reduced manual dexterity are common symptoms associated with diabetes. Visual impairment is estimated to affect at least 16% of patients with type 2 diabetes older than age 65 years and 27% of patients by age 75 years.¹⁰ At least 50% of patients with type 2 diabetes have limited joint mobility in their hands,¹¹ and 25% have symptomatic peripheral neuropathy.¹² For patients with such disabilities, correctly holding a syringe or seeing sufficiently to accurately draw the required amount of insulin may be problematic.

For children and adolescents with diabetes, there are many barriers to achieving optimal glycemic control with insulin therapy. A key issue is titrating insulin therapy to the tight recommended glycemic targets. In this age group, it is particularly difficult to titrate insulin because of the increased risk and fear of hypoglycemia.¹³⁻¹⁵ In addition, for many children with diabetes, doses of insulin required are lower than those for adults, with a higher rate of hypoglycemia observed in children. In part, this may be caused by the increased percentage error in administering small quantities of insulin.¹⁶ Problems injecting small quantities of insulin and administering insulin accurately are identified when using a syringe and vial.¹⁷

The specific needs of elderly patients with diabetes must also be considered when prescribing insulin. Nearly half of

all patients with type 2 diabetes are older than age 65 years.¹⁸ Therapeutic intervention in the elderly must not only accommodate comorbidities and psychosocial changes associated with aging but must also consider that episodes of hypoglycemia can have particularly serious clinical consequences in this age group.¹⁹ Administration of exogenous insulin with consistent reproducibility using a syringe and vial is difficult.¹⁷ Such a problem may be exacerbated by age-associated visual and manual dexterity disabilities.

Pen Devices Address Many Barriers to Insulin Initiation

The advent of pen devices addresses many of the mechanical barriers associated with administering insulin using a syringe and vial. Since the launch of the first insulin pen in the mid-1980s, the administration of insulin has become increasingly simplified.²⁰ The key advantages associated with the use of insulin pens include improved patient acceptability and compliance,²¹ reduced injection pain,²² increased convenience and lifestyle flexibility, greater reliability and accuracy of dosing,^{21,23,24} and simplification of insulin administration. These benefits have been seen in previously insulin- (and pen-) naive patients,²⁵ in children and elderly populations,^{23,26-28} and in those patients with visual²⁹ or dexterity³⁰ disabilities.

What Features Are Important When Choosing an Ideal Insulin Pen?

An insulin pen device suitable for a wide range of patient populations with diabetes can be evaluated by several criteria: (1) ease of use, (2) ease of learning, (3) pen features, and (4) social factors that influence pen use (Table 1). A recently published study assessed the usability, specific pen features, and patient preference of 4 prefilled disposable insulin pens: Lilly Disposable pen (Humalog/Humulin pen; Eli Lilly and Company, Indianapolis, Indiana), Novolog FlexPen (Novo Nordisk, Bagsvaerd, Denmark), a prototype pen (Pen X), and SoloStar (sanofi-aventis, Paris, France).³¹ The FlexPen, SoloStar, and Lilly Disposable pen are shown side by side in Figure 1.

Ease of Use

Several studies have demonstrated that ease of use is an important criterion for the ideal pen user. A recent study assessed acceptability of the HumaPen Ergo (not

Table 1

Subjective Criteria Used to Assess Prefilled Insulin Pen Devices³¹

Features	
Design and esthetics	Usability
Exterior design and styling	Ease of use
Size and portability	Ease of setting the dose
How well the cap fits onto the pen	Ease of reading the dose
Tactile feel and features	Ease of correcting the dose if overdialed
	Auditory feedback
	Number of turns to set dose
	How far the dose button sticks out
	The effort required to inject the dose
	Ease of determining whether the dose was delivered
	Ease of determining the amount of insulin left in the cartridge

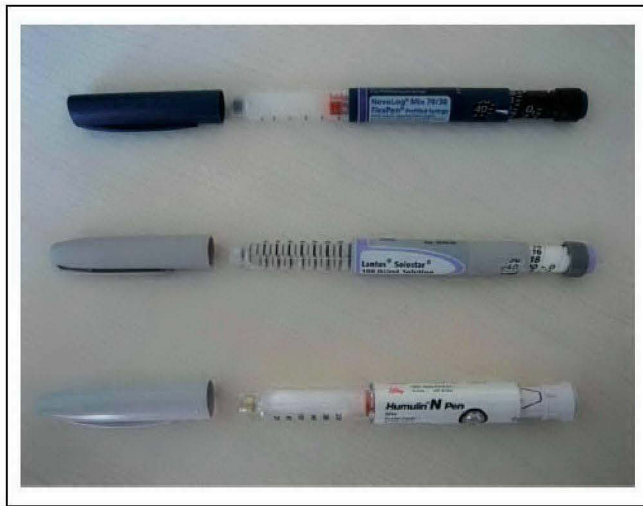


Figure 1. The FlexPen, SoloStar, and Lilly Disposable pen.

available in the United States), a reusable injection pen launched in 1998 by Eli Lilly and Company, which contains replaceable 3.0-mL (300-U) cartridges of insulin. The study showed that in 228 patients with type 1 or type 2 diabetes and 13 health care professionals who were assessed on the acceptability of the HumaPen Ergo, ease of use was considered a reason for recommending the HumaPen Ergo to insulin-requiring patients by 55% of patients and 52% of health care professionals.³²

In a study by Haak et al,³¹ which investigated the usability of the new SoloStar device, FlexPen, and Lilly Disposable pen in 510 patients with type 1 or type 2 diabetes, patients were assessed on their ability to correctly complete a variety of tasks involved in using each pen, including the following:

- Getting started and removing the cap
- Attaching a needle
- Setting (including activation of the dose knob with the Lilly Disposable pen) and delivering a safety dose
- Dialing a 40-U dose and delivering that dose

The assessed steps (excluding the safety step or attach needle step, which was deemed independent of the device) for the SoloStar and FlexPen devices were correctly completed by a similar proportion of patients: 94% for SoloStar and 90% for FlexPen; however, fewer patients correctly completed the same steps with the Lilly Disposable pen (61%). Patients were then asked to rate their preference for each pen based on various usability features. The feature “easy/intuitive to figure out how to use” was most frequently rated as best for SoloStar (55% of the time) and least frequently for the Lilly Disposable pen (13%). The FlexPen was rated as best for “easy/intuitive to figure out how to use” 32% of the time.³¹

In elderly patients, ease of use is an important consideration when recommending an injection device; a complicated

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regimen that the patient does not find easy to use may reduce patient compliance and could lead to inaccurate dosing. In a 12-week study of patients aged older than 60 years with diabetes, patients were assessed on their ability to use a syringe and vial versus an insulin pen. Patients were randomly assigned to administer insulin for 6 weeks using 1 of the 2 methods and then switched to the other method. In total, 90% of patients found the insulin pen easy to understand and preferred it for future treatment because it was faster and easier to use compared with the conventional syringe and vial method.²⁷

In the study by Haak et al,³¹ a high proportion of patients aged 60 years or older correctly completed the assessed steps with the SoloStar (90%) and FlexPen (83%) compared with the Lilly Disposable pen, for which the assessed steps were correctly completed by only 47% of patients. A similarly high proportion of patients with dexterity (91%) and visual (94%) impairments correctly completed all steps analyzed with SoloStar, which was similar to that observed with the FlexPen (84% of patients with dexterity and 89% of patients with manual impairment). In contrast, only half of all patients with either dexterity (52%) or visual (52%) impairments correctly completed all analyzed steps with the Lilly Disposable pen.

Ease of Learning How to Use a Pen

Ease of learning how to use a pen is an important criterion for all patient populations and is particularly important for ensuring early acceptance of insulin therapy in previously insulin-naïve patients, elderly patients, and those patients with visual or manual dexterity disabilities. Assessment of the HumaPen Ergo in patients with type 1 or type 2 diabetes and by health care professionals found that ease of learning was a key feature, making the pen superior to other devices. Indeed, 23% of patients and 18% of health care professionals rated ease of learning as a reason for recommending the pen to other patients requiring insulin.³²

In another study, pen-naïve patients with type 1 or type 2 diabetes who were experienced in administering insulin using a syringe and vial were randomly assigned to 4 weeks of insulin therapy using either a prefilled, disposable pen device (FlexPen) or a syringe and vial, followed by 4 weeks of using the other injection device. Results indicated that more patients expressed a preference for the pen versus the syringe and vial. Among the criteria that contributed to patient preference was ease of use: 74% of patients found the pen device easier to use

overall compared with 21% of patients who preferred the syringe and vial.²⁵

The recent Haak et al³¹ study investigated the proportion of insulin-naïve patients (n = 232) who were able to correctly use 3 pens without tuition (although instruction manuals were available). A similar proportion of patients correctly used SoloStar and FlexPen for the first time (90% and 83%, respectively); however, a lower proportion correctly used the Lilly Disposable pen for the first time (52%). The ease of teaching and ease of use of SoloStar have also been evaluated in a 3-month observational survey of clinical practice, in which physicians and people with type 1 or type 2 diabetes reported that SoloStar was easy to teach³³ and easy to use.³⁴

Dial Features: Dialing Specific Doses, Reading Dial Numbers, and Dialing Back

The literature suggests that ease and accuracy with which patients can dial specific doses are important criteria for a good injection device. As pen devices are more accurate than insulin syringes for the measurement of low insulin doses (<5 U), they are preferred when dialing small doses accurately. This is an important criterion, particularly for children.²³ Accuracy and reliability of the dose setting are also important criteria for patients with visual impairment. Fox and colleagues³⁵ tested 86 insulin-naïve visually impaired patients with type 2 diabetes for their ability to handle 3 different insulin delivery devices; patient preference for each device was also assessed. Results indicated that a device with a clear dose scale, audible clicks accompanying the dialing of each dose, a large dose delivery button, and comfortable to handle device are important features for patients with visual disabilities. The study concluded that a device that is designed to simplify the accuracy and reliability of insulin delivery can improve patient ability to set and deliver correct doses on a repeated basis.

Another randomized, multicenter, crossover trial comparing the FlexPen and HumaLog pen (Eli Lilly and Company) in patients with type 2 diabetes found that 96% of patients believed it was very or rather important that the dose scale was easy to read.³⁶ The 2 most common reasons why the HumaLog pen was rated as worth recommending to an insulin-requiring patient by patients with diabetes or health care professionals were “ease of reading numbers in the dose window” (68% and 74%, respectively) and “easy to dial back without wasting insulin” (77% and 80%, respectively).³²

An evaluation of specific pen features for SoloStar, FlexPen, and the Lilly Disposable pen showed that the proportion of times each pen was rated best for “easy to set dose” was much higher for SoloStar (51%) compared with either FlexPen (29%) or the Lilly Disposable pen (11%).³¹ Similar trends were observed with “ease of correcting dose if overdialed,” for which SoloStar was rated best 50% of the time, compared with 33% for FlexPen and 16% for the Lilly Disposable pen.

Social Issues: Flexibility, Convenience, and Quality of Life

To improve patient acceptance of their treatment and consequently improve patient compliance, the literature suggests that a key criterion for an insulin pen is its impact on quality of life, including flexibility and convenience.

A recent survey carried out in patients with type 1 or type 2 diabetes in the United States assessed patient preferences for the syringe and vial or an insulin pen device. Forty-one percent of patients were insulin experienced, and 59% were insulin naive.³⁷ Results suggested that patients preferred the insulin pen device, regardless of previous insulin experience, with social acceptability the strongest predictor of preference for the device.

Another study investigated patient acceptability of FlexPen based on previous treatment experience in patients with type 2 diabetes (including insulin-naive patients; insulin-experienced, pen-naive patients; and pen-experienced patients). Investigators found that respondents rated FlexPen significantly more positively than their prior treatment strategy, regardless of previous treatment or pen experience; the FlexPen was associated with improved convenience, flexibility, and perceived clinical efficacy and quality of life compared with previous regimens.³⁸

In the study by Haak et al,³¹ patients were asked to evaluate the pens for size and portability. SoloStar and FlexPen were rated as best for these features by 42% and 40% of patients, respectively, whereas the Lilly Disposable pen was rated best for these features by only 22% of patients.

Conclusions

Insulin delivery devices provide a simple and more convenient method to administer insulin compared with

use of a syringe and vial. Use of insulin delivery devices also addresses many of the barriers to insulin therapy in patients with diabetes. A number of criteria should be considered when identifying the ideal pen. Ease of learning how to use an insulin pen, dialing specific doses, and issues of flexibility and convenience are several criteria that must be considered with individual patients before prescribing a particular device.

References

1. DCCT. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. The Diabetes Control and Complications Trial Research Group. *N Engl J Med.* 1993;329:977-986.
2. UKPDS. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study Group. *Lancet.* 1998;352:837-853.
3. Nathan DM, Buse JB, Davidson MB, et al. Management of hyperglycemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement from the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes Care.* 2006;29:1963-1972.
4. Riddle MC. Timely initiation of basal insulin. *Am J Med.* 2004;116(suppl 3A):3S-9S.
5. Cryer P, Childs BP. Negotiating the barrier of hypoglycemia in diabetes. *Diabetes Spectrum.* 2002;15:20-27.
6. Korytkowski M. When oral agents fail: practical barriers to starting insulin. *Int J Obes Relat Metab Disord.* 2002;26:S18-S24.
7. Riddle MC, Rosenstock J, Gerich J. The treat-to-target trial: randomized addition of glargine or human NPH insulin to oral therapy of type 2 diabetic patients. *Diabetes Care.* 2003;26:3080-3086.
8. Raslova K, Bogoev M, Raz I, Leth G, Gall MA, Hancu N. Insulin detemir and insulin aspart: a promising basal-bolus regimen for type 2 diabetes. *Diabetes Res Clin Pract.* 2004;66:193-201.
9. Stewart K, Wilson M, Rider J. Insulin delivery devices. *J Pharm Pract.* 2004;17:20-28.
10. Klein R, Klein BE, Moss SE. Visual impairment in diabetes. *Ophthalmology.* 1984;91:1-9.
11. Starkman HS, Gleason RE, Rand LI, Miller DE, Soeldner JS. Limited joint mobility (LJM) of the hand in patients with diabetes mellitus: relation to chronic complications. *Ann Rheum Dis.* 1986;45:130-135.
12. Ziegler D, Gries FA, Spuler M, Lessmann F. The epidemiology of diabetic neuropathy. DiaCAN Multicenter Study Group. *Diabetes Med.* 1993;10(suppl 2):82S-86S.
13. Bhatia V, Wolfsdorf JL. Severe hypoglycemia in youth with insulin-dependent diabetes mellitus: frequency and causative factors. *Pediatrics.* 1991;88:1187-1193.
14. Limbert C, Schwingshandl J, Haas J, Roth R, Borkenstein M. Severe hypoglycemia in children and adolescents with IDDM: frequency and associated factors. *J Diabetes Complications.* 1993;7:216-220.
15. Mohn A, Dunger D. Insulin therapy in children and adolescents with type 1 diabetes. *Curr Paediatrics.* 1999;9:158-163.

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