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SYMPOSIUM

Practical Aspects of Insulin Pen Devices

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Abstract

Insulin pen devices have several advantages over the traditional vial-and-syringe method of insulin delivery, including improved patient satisfaction and adherence, greater ease of use, superior accuracy for delivering small doses of insulin, greater social acceptability, and less reported injection pain. In recent years, pens have become increasingly user-friendly, and some models are highly intuitive to use, requiring little or no instruction. Despite this progress, uptake of these devices in the United States has not matched that in many other areas of the world. There is a need for improved awareness of the current characteristics of insulin pen devices among United States health care professionals. Knowledge of the design improvements that have been incorporated into pens, both to address patient needs and as a result of the improved technology behind the device mechanics, is essential to promoting the use of insulin pen devices. This review highlights some of the practical aspects of pen use and discusses the factors to be considered when selecting among different insulin pens.

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Introduction

Numerous studies have shown that insulin pen devices have several advantages over the traditional vial-and-syringe method of insulin delivery, including improved patient satisfaction and adherence, greater ease of use, and superior dosing accuracy.[1–7] Despite these advantages, the use of insulin pen devices in the United States remains low compared with other developed countries.[8] About two-thirds of insulin prescriptions in Europe and about three-quarters in Japan are for pen devices.[9] In contrast, in the United States, only 15% of patients are thought to use insulin pens.[10]

Possible reasons for the low adoption rates in the United States include lack of awareness among health care providers of the advantages of pens compared with the vial and syringe.[8,11] An additional issue is the greater prescription cost of insulin cartridges and prefilled insulin pens compared with insulin vials, although the cost to the patient may be the same depending on their coverage; in fact, if they have one copay per box of pens, the cost to the patient may actually be less per unit of insulin. It should be noted, however, that despite the higher unit cost of insulin in pen devices versus vials, several studies have found that overall diabetes-related treatment costs are lower with pen devices than with vial and syringe.[1,2,12] In addition, most pen devices have good formulary coverage. For example, the FlexPen® prefilled pen is covered on more than 90% of managed care plans.[13] Therefore, in theory, costs should not prevent the use of these devices.[14] However, many smaller health maintenance organizations and state Medicaid plans may require prior authorization for insulin pens.

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Given the clinical, practical, and potential health economic advantages of insulin pens, there is a need for improved awareness of insulin pen devices among U.S. health care professionals. A study of patients with type 2 diabetes in the United States found that the physician's role in presenting the pen as an option and recommending pen use was a critical factor in patients' use of pens.[15] Physicians, nurses, and diabetes educators should therefore become familiar with the various insulin delivery devices available so that they can discuss the potential benefits of these devices with patients and offer advice on which device best meets an individual patient's needs. Nurses, diabetes educators, and pharmacists have a particularly important role in educating patients on how to use insulin pens because incorrect use can affect pen performance and thus the accuracy of the administered dose.[16] This review describes the practical aspects of insulin pen devices, including considerations when selecting among different insulin pens.

Advantages of Pen Devices Compared with Vial and Syringes

The traditional route of subcutaneous insulin administration has been the vial and syringe. However, this method of administration has many disadvantages, including fear of injections, poor dose accuracy, lack of social acceptance, lengthy training time, and difficulty of transportation. These factors can all act as barriers to insulin therapy, impacting on lifestyle flexibility and negatively influencing treatment adherence, patient self-management behavior, and achievement of euglycemia.[17,18] Insulin pens have been developed to help address these issues, with resulting improvements in portability, dosing accuracy, mealtime flexibility, and convenience of delivery.[4–6,19] Increased patient preference, treatment satisfaction, and quality of life have been reported for pen devices compared with the vial and syringe;[3,7,20,21] these benefits may be particularly important due to their demonstrated impact on patient adherence. Other studies have shown that pen devices are associated with improved costs of care, less reported injection pain, and improved patient self-management behaviors, including adherence to treatment, compared with the vial and syringe.[1,22–24] Because of the greater ease of use of insulin pens, people with visual impairment or reduced dexterity may especially benefit from using an insulin pen rather than a vial and syringe.

Once in use, most insulin analog vials, cartridges, and prefilled pens must be discarded after 28 days. This means that many patients who use a 10-ml vial end up either wasting insulin or using insulin beyond its recommended discard date. This is rarely a problem for patients using either a 3-ml prefilled pen or a reusable pen containing a 3-ml insulin cartridge. Exceptions to the 28-day discard date are insulin detemir (vials and pens), which can be kept for up to 42 days once in use; biphasic insulin aspart 70/30 prefilled pens, which must be discarded after 14 days; and cartridges and prefilled pens containing biphasic insulin lispro premixes, which must be discarded after 10 days.

Two open-label, randomized, crossover studies have examined whether patients have greater dose confidence with a prefilled insulin pen or with a vial and syringe; both studies found that patients preferred the pen over the vial and syringe in this regard.[3,25] In the first of these studies, 73% of patients felt more confident in the accuracy of the insulin dose delivered with the pen (original FlexPen) compared with 19% for the vial/syringe.[3] In the other study, 88% of patients had greater confidence that they were taking the right dose with the pen (KwikPen®) than with the vial and syringe.[25] A more detailed discussion on the benefits of pen devices over vial and syringe can be found in the article by Selam[26] in this issue of *Journal of Diabetes Science and Technology*.

Available Insulin Pen Devices

Two types of insulin pen are available: prefilled disposable pens and refillable pens (**Table 1**).[27–44] Most insulin pens are proprietary devices, manufactured by Eli Lilly, Novo Nordisk, and sanofi-aventis, and are designed to work with specific insulins from the same manufacturer. All currently available pens either are prefilled with 3 ml (300 units) of insulin or are refillable pens designed for use with 3-ml insulin cartridges (pens taking 1.5 ml insulin were formerly available). Insulin cartridges or prefilled disposable pens are available for all insulin analogs (rapid-acting, long-acting, and premixed) and for most human insulins (**Table 1**).

For all insulin pen devices, a separate prescription for pen needles is required. Pen needles are available from various manufacturers (Allison Medical, BD, Can-Am Care, Delta Hi-Tech, Medical Plastic Devices, Novo Nordisk, Owen Mumford, UltiMed) and come in gauges ranging from 29 to 32 gauge and in lengths from 5 to 12.7 mm.[45] More recent developments have resulted in the introduction of safety needles with protective shields that not only reduce needle-stick injuries but may also allay patient anxieties about needle use.[46] These are discussed in more detail in the section entitled "Individualizing Insulin Treatment with Pen Devices."

Table 1.
Insulin Pen Devices Currently Available in the United States.[a, 27–44]

Product name	Insulin type	Dose range (unit)	Increment (unit)	Recommended needle type[b]	Dialing feature	Other features
Prefilled disposable insulin pens						
Humalog® KwikPen®	Insulin lispro and insulin lispro protamine suspension	Maximum dose 60 units	1	BD Ultra-Fine™ needles	Dial-back feature Cannot dial more than the amount of insulin remaining	Light and portable
Original Humalog® pen Humalog® Mix75/25™ pen Humalog® Mix50/50™ pen	Insulin lispro Insulin lispro protamine suspension/insulin lispro injection	Maximum dose 60 units	1	BD Ultra-Fine needles	Dial-back feature After full dose is delivered, an arrow or diamond is centered in dose window Cannot dial more than the amount of insulin remaining	
Humulin® N pen Humulin® 70/30 pen	Human insulin isophane suspension Human insulin isophane suspension/human insulin injection	Maximum dose 60 units	1	BD Ultra-Fine needles	Dial-back feature After full dose is delivered an arrow or diamond is centered in the dose window Cannot dial more than the amount of insulin remaining	
Lantus® SoloSTAR® Apidra® SoloSTAR®	Insulin glargine Insulin glulisine	Maximum dose 80 units	1	BD Ultra-Fine needles	Dial-back feature Cannot dial more than the amount of insulin remaining	The two pens are distinguished by color, and the Apidra SoloSTAR has a raised dot on the push button
Levemir®FlexPen®[c] Novolog® FlexPen®[c] Novolog® Mix 70/30 FlexPen®[c]	Insulin levemir Insulin aspart Insulin aspart protamine suspension/insulin aspart	Maximum dose 60 units	1	NovoFine or NovoTwist needles	Dial-back feature Cannot dial more than the amount of insulin remaining	Little force required, dose delivery is confirmed by audible click, different insulins color coded, only pen with all three types of insulin analogs Raised dot on push button
Refillable pens						
Autopen® classic	Insulin lispro protamine suspension/insulin lispro injection	Maximum dose 21 or 42 units	1 or 2 unit models available	Compatible with all pen needles	Dial back not possible	Side-mounted release button that is pushed the same minimal distance to inject, regardless of the dose size and the needle gauge
Autopen 24®	Insulin glargine Insulin glulisine	Maximum dose 21 or 42 units	1 or 2 unit models available	Compatible with all pen needles	Dial back not possible	The two dosing models are distinguished by color
HumaPen® LUXURA™ and LUXURA™ HD[d]	Insulin lispro Insulin lispro protamine suspension/insulin lispro injection	Maximum dose 60 units or 30 units (HD)	1 or 0.5 (HD) (minimum dose 1 unit)	BD Ultra-Fine needles	Dial-back feature	Relatively heavy; long reach needed for large doses

Continued →

Table 1. *Continued*

Product name	Insulin type	Dose range (unit)	Increment (unit)	Recommended needle type[b]	Dialing feature	Other features
Refillable pens						
HumaPen® Memoir™	As HumaPen LUXURA	Maximum dose 60 units	1	BD Ultra-Fine needles	Dial-back feature	Digital display and memory of last 16 doses, including priming doses (i.e., eight injections) Relatively heavy; long reach needed for large doses
NovoPen® 3	Insulin aspart Insulin levemir Insulin aspart protamine suspension/insulin aspart Human insulin isophane suspension	Maximum dose 70 units	1	NovoFine needles	NovoPen 3 dial back requires partial disassembly	
NovoPen® 4	As NovoPen 3	Maximum dose 60 units	1	NovoFine needles	NovoPen 4 has easy dial back and cannot dial more than the amount of insulin remaining	Large easier-to-read numbers, reduced dose force, dose delivery confirmed by audible click
NovoPen® Junior	As NovoPen 3	Maximum dose 35 units	0.5 (minimum dose 1 unit)	NovoFine needles	Dial back requires partial disassembly	Distinguished from NovoPen 3 by raised circle on push button
OptiClik®	Insulin glargine Insulin glulisine	Maximum dose, 80 units	1	Ypsomed Clickfine™ needles or BD Ultra-Fine needles	Dial-back feature Cannot dial more than the amount of insulin remaining	Dose displayed for 2 minutes

[a] Cartridge delivery capacity is 300 units, unless otherwise stated.
[b] Needle types shown are recommended by the insulin pen device manufacturer. BD Ultra-Fine and Ypsomed Clickfine needles also fit all current insulin pens.
[c] Also known as the improved FlexPen.
[d] Half dose.

How to Use an Insulin Pen

In a study assessing patient and physician acceptability of the prefilled Humulin®/Humalog® insulin pen device, 88% of the 33 physicians who completed questionnaires at the end of the study thought that it took less time to teach patients to use the pen and 73% thought that it took less time to initiate insulin therapy with the pen compared with a vial and syringe.[47] Teaching patients how to use an insulin pen can be summarized in the five main steps shown in **Figure 1**. It should be noted that because of the mechanics of pen devices, insulin can still be flowing out of the pen for several seconds after the button is fully depressed.[11] Patients must therefore keep the device in place with the button pressed in for 5–10 seconds (the stipulated time varies between package inserts of the various insulin pens). For example, SoloSTAR® recommends a longer *in situ* time (10 seconds) compared with the FlexPen (6 seconds).[37,38,41,42] The easiest way to ensure this is to instruct the patient to count to 5 (or 10, if using the SoloSTAR) before removing the needle. If the patient is using more than 50 units of insulin per dose, a good rule of thumb might be to instruct them to count to 10 regardless of the pen they are using to ensure complete absorption of the insulin.

If patients are using a pen that contains an insulin suspension (neutral protamine Hagedorn insulin or an insulin premix), they must carefully roll or tip the pen for the recommended number of times according to the

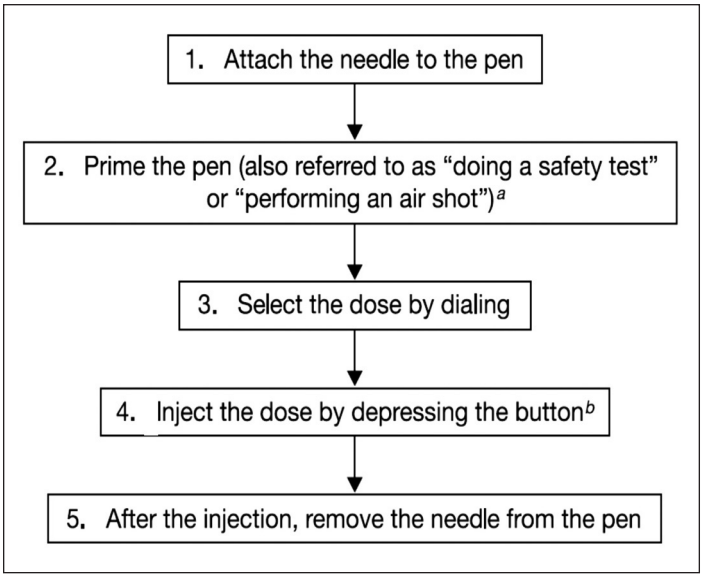

Figure 1. The five steps of insulin pen use. [a] This is performed by instructing the patient to dial up 2 units and to inject these units into the air. [b] The button needs to be pressed and the needle held in the skin for 5–10 seconds to ensure complete delivery of insulin dose. The easiest way to ensure this is to instruct the patient to count to 5 (or 10, if using the SoloSTAR®) before removing the needle.

package insert to ensure even mixing of the insulin suspension before attaching the needle. This issue may be especially important for patients who have used the vial-and-syringe method, as vials have a greater diameter than cartridges and so need to be tipped less often.[48]

Pens must be primed before each injection, and the needle removed immediately after each use.[11] This is performed by instructing the patient to dial up 2 units and inject these units into the air (also called an "air shot"). This will displace any air in the needle and ensure an accurate injection. This air shot may need to be repeated when using a new pen or cartridge until a steady stream of insulin is observed. Insulin pens are manufactured with enough extra insulin to account for this air shot. An insulin pen must never be used by more than one individual, even if the pen needle is changed, because sharing of insulin pens can result in the transmission of hepatitis viruses, human immunodeficiency virus, or other blood-borne pathogens.[49]

Patients and health care workers also need to be aware of the different procedures associated with insulin pens in case of accidentally dialing a dose larger than required. In the case of the Autopen®, the side push-button design makes it impossible to dial back, and care should be taken not to dial past the required dose. With older versions of NovoPen® and NovoPen® Junior, the dose can be adjusted back down by partial disassembly of the pen. This involves pulling the mechanical section and the cartridge holder apart and pressing the dial-up button back to zero. With other pens, namely the SoloSTAR, the improved FlexPen, Humalog KwikPen, original Humalog/Humulin pens, HumaPen® LUXURA™, HumaPen® LUXURA™ HD, HumaPen® Memoir™, OptiClik®, and NovoPen 4, easy dial back is possible by simply reversing the dial-up action.

Prior to first use, the insulin cartridge or pen should be stored in the refrigerator. The pen should be warmed to room temperature [below 86°F (30°C) for most insulin analogs] before use. After use, the pen should remain at room temperature below 86°F (30°C) in order to avoid producing air bubbles, which can form when the pen mechanism and the insulin expand/contract during a temperature change. As with all types of insulin, pens in use should be kept from extremes in temperature, keeping them as close as possible to room temperature below 86°F (30°C) at all times. Insulin glulisine has a narrower temperature range for storage than the other insulin analogs: Once in use, insulin glulisine must be stored below 77°F (25°C). In some buildings, for example, schools, the air conditioning is turned off at night, which may result in the room temperature rising above 77°F (25°C) or 86°F (30°C). Insulated storage packs are recommended in such conditions.

If a patient is switching from one type of insulin pen to another, it is important to check whether the procedure used for the previous pen also applies to the new pen.[50]

Individualizing Insulin Treatment with Pen Devices

Health care practitioners should work with the patient to select insulin delivery devices that are compatible with their insulin regimen, lifestyle, and personal preferences. A regimen that causes the least disruption to the patient's day-to-day life is much more likely to be used. Pens are more than just a matter of convenience, though; their ease of use allows patients to take better care of their own condition.[15] As discussed by Selam[26] and summarized earlier, insulin pens can provide many potential benefits over vial-and-syringe delivery.

Patients across all age groups often have concerns regarding insulin therapy, and many of these concerns can be addressed effectively through choosing an insulin pen device rather than a vial and syringe.[51] In particular, adolescents and children may find insulin pens more socially acceptable because of the pens' greater portability

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