Improved Disposable Insulin Pen Devices Provide an Alternative to Vials and Syringes for Insulin Administration

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The prevalence of diabetes has increased so rapidly during the past 30 years that the condition is now a problem of national importance in the United States. It has been estimated that 12.3% of individuals aged 20–79 years in the United States (26.8 million people) have diabetes, and the vast majority of those have type 2 diabetes.1

Diabetes has devastating effects on patient morbidity and mortality that, in turn, place a substantial economic burden on the nation’s health care resources. In 2010, an estimated 231,000 deaths among people aged 20–79 years in the United States were attributable to diabetes, and the mean annual health expenditure per person with diabetes was $7,383.3 Morbidity and mortality and the associated costs of treatment in diabetes are primarily due to hyperglycemia; achieving and maintaining optimal glycemic control is important for both patients with type 1 diabetes and those with type 2 diabetes to reduce the risk of developing long-term complications.2,3

Typically, in patients with type 1 diabetes, glycemic control is achieved from the time of diagnosis with insulin, whereas in type 2 diabetes, the addition of insulin to an initial regimen of oral antidiabetes drugs (OADs) is known to confer benefits in terms of reduced risk of long-term complications.4 However, although the importance of maintaining optimal glycemic control in diabetes is well documented, insulin therapy is widely underused in the United States,3 largely because a number of barriers to initiation of and adherence to insulin therapy exist such as fear of injections (including self-injection).6,7

Insulin pen delivery devices such as the SoloSTAR (sanofi-aventis, Paris, France), the FlexPen (Novo Nordisk A/S, Bagsvaerd, Denmark), and the KwikPen (Eli Lilly, Indianapolis, Ind.) are generally recognized as being easier to use and more convenient, with improved medication adherence compared to traditional vial-and-syringe delivery.8,9 However, despite the advantages of insulin pen devices, their acceptance and use in the United States has been slower than in Europe and Japan.10–12 This article reviews the benefits and limitations of patient self-administration of insulin with disposable insulin pens currently marketed in the United States across a range of different populations.

Insulin Pens Are a Preferable Method of Delivery for Insulin Self-Administration

The development of insulin pens during the past decade has simplified the administration of insulin,13 making insulin delivery both easier and more accurate. These devices address many of the limitations associated with vials and syringes, including the need to carry bulky equipment, the time and practice required to develop correct syringe technique, and the potential stigma of drawing up an insulin dose and self-injecting in social settings.14,15

Demonstrated advantages of insulin pens over vial-and-syringe delivery include greater patient acceptability and compliance;9 improved health-related quality of life,16 which may be related to less
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Injection pain; increased lifestyle flexibility and greater dosing accuracy, thus decreasing the risk of over- or underdosing and subsequent hypo- or hyperglycemia; and improved ease of use, which positively influences patients’ adherence to their insulin regimen. In small-scale studies conducted in the late 1980s, patients provided with the NovoPen (the first insulin pen to be introduced) preferred using this device to other approaches, including the use of vials and syringes and continuous subcutaneous insulin infusion (insulin pumps).

Insulin Pens May Be Beneficial in Difficult-to-Treat Patient Populations
The benefits of insulin pens have been demonstrated across a range of patient populations, including elderly individuals, patients with visual or dexterity impairments, children, and insulin-naive patients.

Older patients
Nearly half of all patients with type 2 diabetes are ≥ 65 years of age, making older patients the largest population receiving diabetes treatment. The poor dosing reproducibility and inaccuracies of vial-and-syringe delivery represent a particular problem for older patients, who are at a higher risk of hypoglycemia. Therefore, treatments for older individuals must be carefully considered in light of the comorbidities and psychosocial changes associated with aging.

The results of a study conducted by Coscelli et al. in patients ≥ 60 years of age demonstrated that the majority (90%) of patients found the functioning of the insulin pen easy to understand and preferred it for future treatment over the conventional vial-and-syringe method. In a more recent population-based study of residents in Ontario, Canada, who were ≥ 66 years of age and who received a first prescription for insulin between 1998 and 2006 (n = 47,810), 72% of patients began using insulin pen devices, increasing from 46% in 1998 to 86% in 2006, indicating increasing acceptance.

Patients with visual impairment or reduced manual dexterity
Many patients with diabetes have visual impairments or reduced manual dexterity and, as a result, may find correct dose administration with a vial and syringe to be problematic. At least 16% of patients with type 2 diabetes ≥ 65 years of age and 27% of patients > 75 years of age are thought to have visual impairments. At least 50% of patients with type 2 diabetes have limited joint mobility in their hands, and 25% have symptomatic peripheral neuropathy.

Patients with visual impairment and diabetes are naturally subject to certain limitations when using insulin pens. Novo Nordisk states that its FlexPen devices are “not recommended for the blind or severely visually impaired without the assistance of a sighted individual trained in the proper use of the product.” Similarly, Eli Lilly states that its KwikPen is “not recommended for use by the blind or visually impaired persons without the assistance of a person trained in the proper use of the product.” There are no such warnings associated with the sanofi-aventis SoloSTAR device.

Because there are different degrees of visual impairment ranging from moderately impaired to completely blind, a clinical decision must be made as to which pen device is most suitable for a particular patient and whether it can be used without the assistance of a person trained in its proper use who is not visually impaired. The main risks are an inability to measure and deliver doses as accurately as sighted patients, and additional issues could arise when priming the pen. The next generation of pens, currently in development, will offer dose-setting mechanisms with visual, audible, and tactile feedback that could assist visually impaired patients with self-administration. For now, injection devices with easily readable dose scales and easy-to-handle dose selectors are preferable for those patients in whom coordination or vision is suboptimal.

Children and adolescents
Even in the absence of diabetes-related complications, the administration of insulin using a vial and syringe can be problematic in children and young adults. Tight glycemic control is particularly difficult to achieve in younger patients owing to compounding endocrine, behavioral, and social factors, and, as a result, these patients have the worst adherence to insulin injections and dose adjustments. Children with diabetes usually require much lower insulin doses than adults, and it has been proposed that at least some of the episodes of hypoglycemia in children can be attributed to the increased relative error at small insulin doses. Indeed, in one study, the absolute error in measuring insulin doses of < 5 units was nearly 10%.

Insulin-sensitive patients
The ability to administer a small dose of insulin is also important in some populations, such as children with type 1 diabetes and extremely insulin-sensitive patients who need to administer small, precise doses. Although the Luxura HD pen by Eli Lilly can deliver half-unit doses, current disposable pen devices continue to administer doses in 1-unit increments only. Patients would benefit from more pen devices that can deliver half-unit increments.

Insulin-naive patients
Ease of use is an important criterion for patients who are insulin-naive to promote the early acceptance of insulin therapy and overcome barriers to initiation of and adherence to insulin therapy, such as the fear of injections (including self-injection), the inconvenience of vials and syringes, and the risk of hypoglycemia.

Several Available Pens Meet Rigorous Criteria for Ease of Use, Accuracy, and Safety
The benefits of prefilled disposable pens have been established in a number of studies.

Usability assessments
The usability of disposable insulin pens has been demonstrated across a range of patient populations, includ-
ing in children 11–15 years of age and in elderly patients ≥ 60 years of age.47,49 Fischer et al.47 evaluated features of the SoloSTAR, the original FlexPen, the original Eli Lilly disposable pen, and a prototype pen (not discussed here) in an open-label study of 150 U.S. patients with type 1 or type 2 diabetes. SoloSTAR was most frequently rated best by the patients for pen features, including three out of four attributes relating to design and aesthetics, and nine usability (Table 1). SoloSTAR and FlexPen devices were found to be very usable by both pen-experienced patients (98 and 93%, respectively) and pen-naive patients (89 and 82%, respectively).47 Usability in difficult-to-treat patients such as elderly patients, children and adolescents, and those who are visually or dexterously impaired has been shown to be consistent with the overall patient experience, with these patients favoring the SoloSTAR and FlexPen over other devices tested.47

Dosing accuracy
A number of studies have investigated the dose accuracy of disposable insulin pens.50–56 The accuracy of SoloSTAR and both the original and improved FlexPen (also known as the Next Generation FlexPen) are comparable at several clinically relevant doses.54–56 In a clinical setting, SoloSTAR allowed people with type 1 or type 2 diabetes to administer insulin glargine and insulin glulisine with a dose accuracy similar to that achieved in laboratory conditions.55 Greater patient confidence in dose accuracy has been reported with the original FlexPen and the KwikPen compared to vial-and-syringe delivery,28,57 patient-confidence comparative data with SoloSTAR are not yet available.

Injection force
In general, the required injection forces are low for disposable insulin pens.53,58,59 The Next Generation FlexPen reportedly requires 30% less force than the original version60 and was reported to have a significantly lower injection force compared to SoloSTAR.61 However, more recent data comparing the original FlexPen,

<table>
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<tr>
<th>Evaluation of Pen Features: Percentage of Time Rated as Best</th>
<th>SoloSTAR A</th>
<th>FlexPen B</th>
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<tr>
<td>Design/aesthetics</td>
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<tr>
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<tr>
<td>Easy to determine amount left in cartridge</td>
<td>49&lt;sup&gt;B&lt;/sup&gt;</td>
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<td>35</td>
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</tbody>
</table>

Letters denote statistical significance over the pen with the corresponding letter (P < 0.05). Respondents selected the one pen they considered best on each attribute. Row percentages may total > 100% because some respondents could not select one pen as best and instead opted to note “ties.”
the Next Generation FlexPen, KwikPen, and SoloSTAR reported a significantly lower injection force for SoloSTAR compared to the other disposable pens at maximum doses and dispense rates (P < 0.05), and this was also lower at doses of 60 units. Pens that require low forces to inject insulin and have a short stroke length should be easier for patients to use.53

Suitability for basal-bolus regimens The clinical suitability of a device extends beyond its usability; insulin pens have been shown to be instrumental in avoiding possible treatment mix-ups caused by injecting the wrong insulin,62 a situation particularly relevant to patients using a basal-bolus insulin regimen. A recent study of patients with diabetes in the United States63 sought to evaluate the scope of this problem by providing patients with a pair of pens containing long-acting or short-acting insulin. The study revealed that patients given the SoloSTAR devices were less likely to select the incorrect insulin (2.7%) compared to those given the improved FlexPen (16.3%) and that the pen body color was an important determinant for the lower error rate with the SoloSTAR device,63 even among patients with impaired color vision.64 The improved FlexPen has also been color-coded to allow for clear differentiation between insulin types.65

Insulin Pens Are Underused in the United States Pen devices are popular in Europe and, in many places, their use exceeds that of vials and syringes.10–12 However, insulin pens are reportedly used by <10% of U.S. insulin users.11 Various factors may contribute to the low acceptance rate of insulin pens in the United States. Disposable insulin devices have been freely available on National Health Service prescriptions in some form in the United Kingdom since the early 1980s, with the first NovoPen being introduced to the market in 1984.11 In contrast, insulin pens were not introduced in the United States until 1987, and their use is not universally covered by health insurance carriers. Insulin pens also appear to be slightly more expensive than vials and syringes in the United States.11 In actual terms, in the United States, insulin costs ~23% more per unit with a pen device (14.6 cents) than it does with a vial (11.9 cents based on insulin glargine).66

However, a recent review67 of adherence with vials and syringes compared to insulin pens showed insulin pens to be associated with improved adherence to therapy compared to vials and syringes, and the associated health care resource utilization and total diabetes costs were actually lower with insulin pens than with vials and syringes. Consistent with these findings, a recent study68 that compared glycemic control and health care expenditures of insulin glargine delivered via a pen device or with vials and syringes among patients in a national managed-care database showed that the use of an insulin pen was associated with less frequent treatment discontinuation, greater A1C improvement, lower rates of medical claims for hypoglycemia, and a trend toward lower total medical expenditures.

It is important to consider, however, that increased treatment costs have the potential to affect adherence in patients with inadequate health care coverage. A study69 examining the relationship between health insurance coverage and cost-related medication under-use showed that 40% of patients with no health insurance coverage self-reported poor adherence to their medication.

Physicians’ perceptions of device benefits also play a powerful role in driving the use of insulin pen devices in the United States. Evidence in U.S. patients with diabetes demonstrated that physicians’ recommendations of insulin pen use, physicians’ presentation of insulin pens as an option, and patients’ perceptions that insulin pens facilitate diabetes self-care and are not costly are instrumental in pen uptake.70 However, insulin pens generally seem to be viewed as a tool only for patients who require intensive management.71 Misconceptions about the ease of teaching pen injection technique may also exist, particularly because saline pens are not available for teaching purposes in the United States.71

Limitations to Patient Self-Administration With Insulin Pens There is a wealth of clinical and economic evidence to show the many advantages to using insulin pen devices in diabetes management in the United States. However, it is important to remember that pens do have certain limitations that must be considered before prescribing their use for self-administration.

Besides having a higher cost per unit than insulin supplied in vials,66 the main limitation to insulin pen use is that patients are unable to mix their own insulin formulations, although there are some premixed biphasic insulin analog preparations available in prefilled pens. In addition, care must be taken when using different pens for different insulins to ensure the correct insulin type is used at the correct time. As described above, disposable insulin pen devices such as SoloSTAR and the improved FlexPen currently use color to distinguish between rapid- and long-acting insulins, although this may not be sufficient for patients with visual impairment. Finally, patients must also possess adequate manual skills and visual acuity to correctly use a pen device.

Conclusions Diabetes is a multifaceted condition affecting a wide variety of people from children to the elderly, including those with varying degrees of disability. The specific needs of these individuals must be taken into account when choosing an insulin administration device.

Insulin pens are relatively simple and convenient devices with which to administer insulin and overcome some of the barriers to insulin therapy in patients with diabetes. Several available pens, including the SoloSTAR, the original and improved FlexPens, and the KwikPen meet a number of important criteria, namely, ease of use, accuracy, and convenience, and could facilitate the administration of insulin and promote self-management as advocated by the American Diabetes Association.71
Improvement in physicians’ and patients’ awareness of the potential benefits of insulin pen use, together with a clearer understanding of the cost implications of prescribing these devices, could drive an increase in future insulin pen use in the United States.

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