Insulin Pens: The Modern Delivery Devices

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Abstract
Strict glycemic control helps in reducing complications and mortality in patients with diabetes. Insulin remains the mainstay in treatment of diabetes. One of the most important barriers to insulin therapy is the use of conventional insulin delivery system, which remains time-consuming, cumbersome, inconvenient and painful. Insulin dosing via syringe is associated with a high risk of dosage errors. The modern pen devices have various advantages over the conventional insulin delivery methods. The user-friendliness and comfort of injection makes the initiation of insulin easier. The ease of use of insulin pens and the flexibility of incorporating insulin injections into a busy lifestyle may improve diabetes control with much less effort, while maintaining the quality of life for the diabetic patients. Reusable and prefilled pens are available.

Introduction and Rationale for the Use of Insulin Pens

The beneficial role of strict glycemic control in people with diabetes has been proven in many large clinical studies and the evidence is getting stronger. There has been a tremendous improvement in the number of patients achieving the target glycemic control. This has been made possible as the result of advances in medical science since the discovery of insulin by Banting and Best in 1921. Insulin has been the mainstay of therapy for all subjects with type 1 diabetes and majority of type 2 diabetic subjects. However, there are several barriers to insulin therapy that need to be addressed. One of the most important barrier is the use of conventional insulin delivery process, which remains time-consuming, cumbersome, inconvenient, and to some extent, painful. Furthermore, insulin dosing via syringe is associated with a high risk of dosage errors, with as many as 80% of patients carrying out some aspect of insulin administration via syringe incorrectly.

Although insulin was discovered almost 9 decades ago, the technology involving the insulin delivery did not see much of change till the introduction of pen device in 1985. The provisions for insulin delivery have come a long way from very crude and inconvenient metal syringes to the modern pen devices with very fine needles for accurate, flexible, convenient, and virtually painless administration. Insulin pens have the potential to become a major asset for breaking barriers to early initiation of insulin as they overcome many shortcomings of their previous counterparts (Table 1). Insulin pens have become extremely popular throughout the world; in some countries, 70% to 90% of all insulin is delivered by pen devices. Insulin pen devices are unique in that they combine the insulin container and the syringe in a single unit. Some of these pen devices feature an audible click on dose dialing, single-unit dose increments, two-way dose setting, large dials showing the selected dose, and automatic return to zero after dialing the full dose. With these state-of-the-art insulin pens, physicians will also find that their efforts are more rewarded, which may hold the key to better long-term outcomes.

Types of Insulin Pens

The 2 types of insulin pens available currently are reusable and prefilled (disposable) pens.

Reusable pens: In reusable pens, an insulin cartridge is inserted into the pen’s delivery chamber. For patients, this allows greater flexibility (i.e., changing types of insulin without a need 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. With individual use of the pen device, the risk of infection is minimized. Examples of such reusable (durable) pens are NovoPen® 3 (for both human and analog insulins), Humapen® (for both human and analog insulins), Optipen®, Autopen® pen, and Wosulin pen. HumaPen® MEMOIR™ comes with a “memory” allowing patients, especially those on multiple mealtime doses, to record and review their last 16 insulin doses, including the priming doses. NovoPen® 4, which is yet to be launched in India, has shown dose accuracy before and after simulation of 5 years of use across a wide range of temperature and humidity conditions and after mechanical challenges. The mean injection force required to operate NovoPen® 4 was reduced up to 50% as compared to that for NovoPen® 3, and the mean dosage display for NovoPen® 4 was over 4 times larger than that for NovoPen® 3. Based on these findings, patients with diabetes who have manual or visual impairment should find it easier to dose insulin with NovoPen® 4. NovoPen® junior and HumaPen®luxura™ HD are 2 innovation designed mainly for young children with diabetes to facilitate dialing at small quantum such as 0.5–1 IU. A large body of published evidence accumulated over the past 2 decades testifies to the patient-related benefits of the NovoPen family of insulin injection devices in the treatment of diabetes. The insulin cartridges fitting durable pens are called penfils. Insulin cartridges for the reusable pens are generally available in 3.0-ml volume (300 units) and are specific
has been built upon the high standards set by the FlexPen® and is continuing to be marketed in some countries from the late 2008 and is continuing to be marketed as insulin delivery devices.6 Dose accuracy with insulin pens was found to be better in many studies in comparison to vials and syringes method especially at low doses (≤5 IU).7,13,14 All patients experienced fewer problems and preferred FlexPen® than Humalog Pen.19 When these pens were compared with respect to dosing error, Humalog pen delivered underdoses in 17.1% and 28.9% at both the 10 IU and 30 U with a standardized protocol, the Next Generation FlexPen® underdosed one dose, whereas SoloSTAR® underdosed three doses.

**Outcomes of questionnaire**

<table>
<thead>
<tr>
<th>Outcome of questionnaire</th>
<th>Favors pen device (%)</th>
<th>Favors syringe device (%)</th>
<th>Favors none (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Easy and quick operability</td>
<td>88</td>
<td>12</td>
<td>00</td>
</tr>
<tr>
<td>Pain experienced during injection</td>
<td>62</td>
<td>02</td>
<td>43</td>
</tr>
<tr>
<td>Easy pre-selection of insulin dose</td>
<td>86</td>
<td>14</td>
<td>00</td>
</tr>
<tr>
<td>Overall acceptability</td>
<td>90</td>
<td>02</td>
<td>08</td>
</tr>
</tbody>
</table>

for the pen size. The *penfils* 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 for a month, as long as it is kept away from direct heat and light.

**Prefilled pens**: Prefilled pens contain a built-in single-use insulin cartridge. Because this device requires no loading by the patient, it is very 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 change cartridges. The examples of reusable pens are NovoLet®, Humajet®, KwikPen®, Optiset®, and SoloSTAR®. The newest of the prefilled pens available for both human and analog insulins is the Next Generation FlexPen® from Novo-Nordisk which has single-unit dosing increments, audible clicks when dialing the dose, a large magnifying window that shows the 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. Currently, it has become the most popular prefilled pen device being used by millions worldwide.6,7

The Next Generation FlexPen®, which has been available in some countries from the late 2008 and is continuing to be launched in countries around the world (including India), has been built upon the high standards set by the FlexPen®. Emphasis has been given towards new features like less injection force easily noticeable labels and packaging to aid insulin type identification and an innovative simple and easy needle attachment with a “just twist” mechanism.6,8,10 These features provide improved convenience and ease of use for people with diabetes.4,5

**Advantages of Insulin Pen Devices: Clinical Evidence**

**Insulin pens vs vials and syringes**

Several clinical studies have evaluated the use of insulin pens since their introduction in 1985. The first clinical study reported that the pen’s advantages outweigh the inconvenience of multiple injections.11 The findings from a study on elderly diabetics favored pen devices over syringes in terms of operability, pain, insulin dose pre selection and overall acceptability (Table 2).3 In a study 74% patients preferred FlexPen® as compared to 20% preferring vials and syringes citing the following as the main reasons for the preference: (i) more discreet to use in public, (ii) ease of reading dose scale and use.12 Many studies have also shown better convenience, flexibility, and quality of life results with pen devices as compared to the conventional insulin delivery devices.8 Dose accuracy with insulin pens was also reported to be better in many studies in comparison to vials and syringes method especially at low doses (≤5 IU).7,13,14 All these factors are important in improving the patient adherence to the treatment and also reducing the hypoglycemic episodes.15

**Comparative Evidence between Available Pen Devices**

It is pertinent to recall the definitions of the following terms before interpreting the findings of various studies comparing the efficacy an accuracy of different insulin delivery devices.

**Injection force**: It is the peak force attained when pushing the dose knob of a pen device during injection. As injection force increases, the user would need to exert proportionately greater effort in self administering a prescribed dose.16

**Glide force variability**: It is the variation of force during steady-state dosing. It is used to quantify “smoothness” of injection as a means of translating a technical measure into clinical application.17

**Dose accuracy**: It is tested in vitro by measuring the delivered doses under reference conditions, such as temperature and relative humidity, on a highly sensitive balance and is corrected for the specific density of the insulin used (according to specification of International organization for standardization (ISO) 11608-1). The precision is calculated from the variance around the mean delivered dose.9 Transition from conventional delivery device to NovoPen® has been found to be associated with more accurate dosing, while the glycemic control was equivalent, and in some cases superior, without increase in the hypoglycemia incidences.17 Confidence in patients’ ability to use the device was reported better with FlexPen® as compared to Humulin® Pen and Optiset® by both patients and physicians.18 In comparative studies, patients experienced fewer problems and preferred FlexPen® than Humalog Pen.19 When these pens were compared with respect to dosing error, Humalog pen delivered underdoses in 17.1% and 28.9% at both the 10 IU and 30 IU doses respectively, whereas FlexPen® delivered all doses within prespecified limits.14 Similarly, dose accuracy was found to be more with FlexPen® with superior glycemic control and without increase in the hypoglycemia incidences.20

In a direct head-to-head comparison of the 2 prefilled insulin pens, Next Generation FlexPen® and SoloSTAR® at a dose of 10 U and 30 U with a standardized protocol, the Next Generation FlexPen® was found to be more accurate than the SoloStar®
at both tested doses. Only 0.2% of the doses were outside the ISO limit at 10 IU with the NG FlexPen (0.6% at 30 IU). The corresponding figures for the SoloStar® were 0.4% and 1.8%, respectively (Figure 1).8

Rissler et al. evaluated force dynamics of Next Generation FlexPen® and SoloSTAR® at 3 different injection speeds (push-button speeds: 4, 6, or 8 mm/s). They found that Next Generation FlexPen® has a significantly lower (18 to 45%) injection force at all speeds, and delivers 60 IU insulin faster (including recommended waiting time) than SoloSTAR®.9 In yet another study by Asakura et al.,21 Next Generation FlexPen® was found to have a significantly lower (p < 0.05) mean injection force than SoloStar® and KwikPen® when tested in vitro at ideal conditions during injection of 20 IU insulin at 3 different speeds such as 3.3, 5, and 8.3 mm/s using either a BD Micro-Fine™ 31G thin-wall needle or a NovoFine™ 32G tip extra thin wall needle (Figure 2). This is the only study comparing head to head the efficacy of 3 frontline modern pens recently introduced in the market.

A review article by Pfützner concluded that Next Generation FlexPen is simple to use and is more accurate than other prefilled pens. NGFP ensures a reduced injection force and allows easy differentiation between insulin types.10

Insulin Pen Devices: Conclusion

The modern pen devices have various advantages over the conventional insulin delivery methods. The user-friendliness and comfort of injection makes the initiation of insulin, hitherto considered a very difficult task, a lot easier. The ease of use of insulin pens and the flexibility of incorporating insulin injections into a busy lifestyle may improve diabetes control with much less effort, while maintaining the quality of life for the diabetic patients.

References


