Insulin pen injector for the treatment of type 1 diabetes mellitus

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Abstract

Objective: the objective of this review was to evaluate the medical literature in the last ten years comparing the use of insulin pen injectors versus insulin syringes in children with type 1 diabetes.

Sources: this is a review of literature in the last ten years based on Medline.

Summary of the findings: the use of the insulin pen injector is disseminated all over the world. Most studies show that this method is more comfortable and makes patients’ life easier. It is associated to better glycemic control, it is more easily accepted and is related to the reduction of hypoglycemic crisis. The use of the insulin pen injector provided better quality of life to this group of patients.

Conclusions: the new technology produces different methods of insulin administration trying to improve the quality of life of diabetic patients and to reduce the risks of short term complications through the use of insulin pen injectors. The effects of this kind of insulin delivery with the aim of preventing chronic complications are not well established.


Introduction

The treatment of type 1 diabetes mellitus (DM) has had some significant breakthroughs over the last few decades. The exogenous administration of insulin has been the only available treatment for millions of diabetics all over the world. After Banting and Best discovered insulin in 1921, the possibility of obtaining an ideal blood sugar level control was more likely, offering diabetics a better survival rate and quality of life.

According to the Diabetes Control and Complications Trial (DCCT), the strict control of blood sugar level reduces the risks for microangiopathy, retinopathy and nephropathy in diabetic patients. The treatment should be conducted on an individual basis and requires the participation of a multiprofessional team, commitment of the patient and help from family members.

The increased number of patients with type 1 diabetes and technological advances have allowed for alternative therapies whose main objective is to offer patients greater comfort and well-being. For many reasons, an artificial sensor capable of providing insulin at physiological levels based on the fluctuation of daily glycemic levels is not available yet. The use of insulin pen injectors comprises approximately 70% of insulin administrations in the United States. This method allows for a better metabolic control,
with greater treatment adherence and better quality of life for the patients.

Between 60% and 80% of diabetic patients who use insulin syringes fail to administer them correctly. The use of pen injectors is associated with higher dose accuracy and, consequently, with safer treatment. These factors contribute to the increased number of insulin pen users.

In the present study, we underscore the importance of blood sugar level control with insulin therapy in diabetic patients by reviewing the literature on this topic available in Medline database in the last ten years. We discuss the new forms of insulin administration available in our country, with special emphasis on the pharmacological aspects, advantages and disadvantages of insulin pen injectors in current clinical practice.

**Therapeutic aspects of insulin**

Approximately 75 years ago, insulin was administered intramuscularly, causing intense pain at the injection site. Nowadays, the vast arsenal of insulin administration techniques allows for easier and more comfortable type 1 DM therapy. The search for new forms of insulin administration has been a lot more intense in the last few years, especially with regard to insulin pen injectors.

In Brazil, insulin preparations consist of U-100 (100 units/ml). Currently, insulin preparations are highly purified, with low rates of allergic reactions, immune resistance and lipodystrophy. In our country, the following types of insulin are available: pork, pork-beef, and human (biosynthetic and semisynthetic).

Cartridges of NPH, regular, premixed (NPH/regular) insulin and very rapid-acting insulin analogs are available for use in insulin pens. We estimate that the refill of very long-acting insulin analogs will soon be available in our country. In addition, there is no cartridge for the mixture of long-acting and very rapid-acting insulin, which is the most recommended at the moment.

Therapeutic success depends not only on the type and dose of insulin, but also on its form of administration. Subcutaneous injections, which are administered on average three to five times a day, are the most commonly used. The introduction of insulin pens provided diabetics with more comfort and mobility, since these pens can be easily transported and used with greater discretion.

Other pharmaceutical forms of insulin have been studied, such as inhaled insulin, insulin tablet, and continuous subcutaneous insulin infusion (CSII) device. Clinical practice has shown that insulin pens are efficient in treating type 1 DM, offering diabetic patients adequate blood sugar level control, reduced risks of hypoglycemia, increased comfort, and better quality of life.

**Insulin pen injectors**

**General aspects and mechanisms of action**

Insulin pen injectors were introduced in the mid-1980’s. They represent a remarkable advance in the form of insulin administration since they optimize the treatment of type 1 diabetes.

Two types of insulin pens are currently available in our country: disposable and reusable pens. Of which, the latter are more commonly used at present. Both types consist of an insulin cartridge or refill with its own needles, which are changed after each application. The improvement of the mechanical quality of reusable insulin pens adds durability and resistance to multiple refilling.

In general, the cartridges contain 1.5 ml (150 IU) or 3.0 ml (300 IU) of NPH human insulin, regular, premixed (NPH/regular) or Lispro analog. The insulin must be stored in a refrigerator until before its use; after that, it can be maintained at room temperature, protected from sunlight and heat. The available needles are smaller than those used in conventional syringes, thus reducing pain at the site of application. After application, the needle must be removed to avoid contamination of the cartridge. This method offers increased dose accuracy, more safety and a higher level of satisfaction.

**Technical aspects of insulin pen injectors**

The use of the insulin pen is associated with ease of handling, dose accuracy and practical application. However, there are some important peculiarities about this form of administration. Some instructions on the use of the insulin pen are presented below:

- Perform a safety test and press the safety button to release the dose knob;
- Dial the dose by turning the knob clockwise;
- Check the selected dose on the dial;
- Pull off the needle cap;
- Choose a site for application and introduce the needle under the skin;
- Press the injection button until it locks;
- Wait for ten seconds;
- Replace the caps and resume the procedure.

For its simplicity and ease of handling, the insulin pen is recommended for children and adolescents, offering dose accuracy, reduced pain at the application site, and discretion.

**Advantages and disadvantages**

In the last years, several studies have tried to confirm the efficacy of injector pens as a tool for insulin administration compared to conventional therapy, in terms of lab standards and quality of life for the patients.
The insulin pen does not require cleaning the insulin bottle or aspirating the adequate dose, making adjustments, such as removing air bubbles from the syringe. The administration is easier, faster, and more convenient for the patient. A study carried out in the United States revealed that 95% of the patients prefer to use the insulin pen.

The anatomical shape of the pen allows for easy transportation and discreet use in public places, such as bars and restaurants. The pen is associated with reduced pain at the application site, increased safety and dose accuracy, which result in better quality of life for diabetic patients. The pen’s dial offers higher dose accuracy and reliability in the treatment.

In current clinical practice, approximately 60 to 80% of the patients fail to proceed correctly when using insulin syringes. In 1998, a study assessed the acceptance of this method as a form of insulin therapy. The use of insulin pens was well-received by the population, especially among adolescents, since the pens give them more freedom and discretion, thus minimizing the psychological and social effects of DM on this age group.

According to literature review, the use of the insulin pen is associated with the reduction of acute adverse effects of DM, offering diabetic patients greater satisfaction with the control of the disease, in addition to a feeling of well-being and increased reliability in the treatment.

The major downside of this new form of insulin administration is the natural wear of the device, which could reduce dose accuracy and compromise efficiency.

Another important factor is concerned with the insulin therapy used. Today, the most frequently recommended treatment consists of the combination of long-acting insulin and varied doses of very rapid-acting insulin. This recommendation is based upon capillary glucose measurements before meals. This kind of treatment has proved highly efficient and requires multiple doses of bolus insulin. The conventional syringe allows mixing long-acting and very rapid-acting insulin, thus reducing the number of necessary injections. In this case, the use of the insulin pen is quite limited, since the insulin used often corresponds to fixed premixed preparations, preventing the variation of the very rapid-acting insulin dose. Therefore, more than one pen and two applications before each meal would be required. This would hamper treatment adherence and would increase procedure costs.

The isolated use of NPH, regular or Lispro analog insulin requires the use of an extra pen or conventional syringe to resume the insulin therapy. This explains the use of fixed premixed insulin preparations in most cases, even with the limitations outlined above. At the present time, a possible alternative is to administer NPH or long-acting insulin with a syringe, once or twice a day, followed by the administration of very rapid-acting insulin with a pen injector in the form of bolus before the meals, based on the patient’s capillary glucose measurements. In this case, the use of two pens increases the costs of treatment and reduces patient’s satisfaction.

We underscore that insulin pens must not be shared, in order to avoid viral infections, as shown by Sonoki et al. (2001). The cost of treatment is a bit higher than that of conventional therapy, and may be a limiting factor, especially in developing countries with scarce financial resources, such as Brazil.

Use of insulin pens in clinical practice

The studies on pen injectors for insulin administration have held the attention of researchers since the 1980’s. Jefferson et al. (1985) compared the effects of this type of administration with the conventional syringe method on adolescents. They observed a reduction of 2% in the level of glycated hemoglobin (HbA1c) in pen users.

In 1995, a similar study assessed the safety and stability of this insulin administration method in patients older than 60 years. Those elderly patients, who suffered from type 1 DM, showed a high level of satisfaction with the method.

Due to the prevalence and predominance of this disease in children, several studies have approached the advantages and disadvantages of insulin pen injectors in this age group. In a recent study, the authors observed higher efficiency, dose accuracy, reduction of hypoglycemic bouts and improvement of the quality of life for the patients after the use of the insulin pen as standard therapy.

The study carried out by Lteif et al. (1999) is the most comprehensive on insulin pens. They assessed the impact of this method on 1,310 adult patients with type 1 and type 2 diabetes. Their conclusion was that dose omission was lower in pen users (85%) than in patients who used syringes (72%). The level of satisfaction and preference in relation to conventional therapy was 77%.

In the state of Minas Gerais, in the southeast of Brazil, the use of insulin pens has been a routine at the Diabetes Weekend, an educational program whose aim is to offer children and adolescents with type 1 diabetes leisure and culture by providing knowledge and allowing the exchange of information between participants. The use of the insulin pen increased after the Diabetes Weekend program. The program showed that the use of the pen is associated with greater acceptance of the disease by the child, ease of administration, ease of handling, more comfort in terms of use and better dose accuracy. According to the participants, the main advantages of this method in relation to the conventional treatment are discretion and safety.

With respect to the prevention of chronic complications of type 1 DM, the effects of the insulin pen delivery system are not clearly defined yet. Therefore, new randomized, multicenter, long-term studies are necessary to assess the impact of this method on late complications and, consequently, on the morbidity and mortality of these patients.
Conclusion

The insulin pen has proved highly efficient, producing a satisfactory clinical outcome, offering ease of use, dose accuracy and safety for the patients. Discretion and ease of use, in addition to an ideal metabolic control, are among the major factors that make this form of insulin administration an alternative to the treatment of type 1 diabetes. New, randomized, long-term studies are necessary to confirm the efficiency of this method in the prevention of chronic complications of diabetes, and assess its impact on the mortality of these patients.

References