



ISSN (E): 2277- 7695  
ISSN (P): 2349-8242  
NAAS Rating 2017: 5.03  
TPI 2017; 6(6): 36-39  
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www.thepharmajournal.com  
Received: 07-04-2017  
Accepted: 08-05-2017

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## The features of insulin pump therapy for treatment of diabetes mellitus

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#### Abstract

Diabetes mellitus is a world-wide problem that causes incessant search for new areas of treatment of this disease. The incidence of diabetes mellitus is rising and expected to rise further, because of an ageing population and an increasing prevalence of obesity. Continuous subcutaneous insulin infusion or insulin pump therapy is recommended as a possible treatment of type 1 diabetes mellitus in children and adults, as well as type 2 diabetes mellitus if the multiple daily injections of insulin or its analogs are not effective, and also in patients with frequent hypoglycemic states. For continuous subcutaneous insulin used external pump that provides a continuous supply of insulin from the reservoir via subcutaneously administered cannula. There are an insulin dose calculator, programmable basal and bolus insulin infusion, different types of infusion sets among options of most insulin pumps. Insulin pump operates using insulin analogues ultrashort action. Insulin pump therapy should only be started by a qualified specialist team, which should provide patient education on the use of insulin pumps, provide advice on lifestyle and physical activities that are appropriate for these patients. Amid continuous subcutaneous insulin infusion the variability of blood glucose significantly was reduced, the glycosylated hemoglobin rate was decreased, the control of the «dawn phenomenon» improved. Insulin pump therapy in patients with the both type of diabetes mellitus improves quality of life.

**Keywords:** diabetes mellitus, glycosylated hemoglobin, insulin pump therapy

#### 1. Introduction

Diabetes mellitus is a chronic metabolic disorder caused by insufficient activity of the hormone insulin and a subsequent loss of control of blood glucose levels. There may be a lack of the hormone itself or resistance to its action. The onset of type 1 diabetes mellitus usually occurs in children and young adults. The incidence has been increasing over time, with the greatest increase in children younger than 5 years. Type 2 diabetes mellitus occurs in adults and usually begins after the age of 40 years. The incidence is rising and expected to rise further, because of an ageing population and an increasing prevalence of obesity. There is also an increasing incidence of type 2 diabetes mellitus in children <sup>[1, 2]</sup>.

Diabetes mellitus can cause short- and long-term complications. Short-term complications are acute metabolic emergencies that can be life-threatening: diabetic ketoacidosis, which is a consequence of high blood glucose levels (hyperglycemia); and low blood glucose levels (hypoglycemia) caused by treatment. Mild hypoglycemia can be corrected by oral intake of sugars. Severe hypoglycemia is defined by the need for assistance from another person for recovery. Severe hypoglycemia can cause convulsions, coma and, very occasionally, death <sup>[2, 3]</sup>. In children, especially those younger than 5 years, severe hypoglycemia can cause long-term cognitive impairment. Fear of recurrent hypoglycemia not only decreases quality of life but can also hinder adherence to treatment and the achievement of good glycaemic control. The long-term microvascular and macrovascular complications of chronically elevated blood glucose levels include retinopathy and blindness, nephropathy and renal failure, ischaemic heart disease, stroke, neuropathy, and foot ulceration and amputation. Uncontrolled diabetes in pregnancy is associated with adverse pregnancy outcomes <sup>[1-4]</sup>.

Diabetes mellitus is a lifelong condition in which both morbidity and treatment affect quality of life. On conventional (that is, injection) insulin regimens daily life activities need to be arranged around a relatively inflexible structure of meal times and insulin injections. Diabetes is a source of stress for all members of an affected person's family and in the case of children can cause intense parental anxiety. As the length of time with diabetes increases and with the onset of complications, people with diabetes may experience occupational difficulties because of disabilities as well as requiring prolonged and frequent medical attention <sup>[1, 4]</sup>.

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The type 1 diabetes mellitus requires lifelong treatment with insulin [13]. Type 2 diabetes mellitus is initially managed by lifestyle change including diet and weight loss, if necessary. If this is insufficient, oral glucose-lowering drugs are introduced. Over time, many people will need insulin to control their blood glucose levels [1, 2].

There are various types of insulin, distinguished by their rate of onset and duration of action. Insulin requirements change depending on food intake, exercise or intercurrent illness. Achieving good control of blood glucose through an intensive regimen reduces the risk of complications. Intensive insulin regimens attempt to reproduce the normal secretion of insulin by the pancreas [4]. However, exogenously administered insulin lacks the feedback mechanism that the pancreas uses to regulate insulin secretion, whereby insulin production decreases as blood glucose levels fall. Therefore, people taking insulin need to check their blood glucose levels regularly by using a monitor (glucometer). Long-term monitoring of control is achieved by measuring glycosylated Haemoglobin (HbA1c) levels, which reflect average blood glucose levels over the preceding 3 months. Good control is indicated by a value of less than 7.0% [1, 4].

### Aim of study

To describe of the features of insulin pump therapy for treatment of diabetes mellitus, their analysis and conclusion.

### Materials and methods

Research, analysis and synthesis of contemporary literary scientific data that reflect the features of insulin pump therapy for treatment of diabetes mellitus.

### Results and discussion

Insulin pumps have been used for more than 35 years. In the USA in 2005, the level of insulin pump penetration was estimated at 20 to 30% in patients with diabetes mellitus type 1 and <1% in insulin-treated patients with diabetes mellitus type 2. The U.S. Food and Drug Administration (FDA) estimated that the number of patients with type 1 diabetes using continuous subcutaneous insulin infusion was approximately 375,000 in 2007, up from approximately 130,000 in 2002. The actual number of patients using insulin pumps in the USA is difficult to ascertain, but has been reported to range from 350,000 to 515,000 [5, 6].

An insulin pump is a complex electronically-controlled device for the continuous subcutaneous infusion of insulin to patient with type 1 diabetes mellitus. Its advantage over multiple daily insulin injections is that patients can deliver more physiological amounts of insulin between meals and at meal times [7].

Insulin pumps are advancing in form as well as function years, they were simply miniature syringe pumps, with all of the pitfalls associated with these devices. Although complex, insulin pumps are now easier and safer to use. Insulin dose calculators ("wizards") are standard features of all current pumps. These improve dosing consistency and may decrease the frequency of insulin "stacking" (i.e., administering an insulin bolus while a recent prior bolus is still active) [4, 6, 8].

However, it is important to recognize device-specific recommendations may differ among patient scenarios. Therefore, prescribers should be familiar with these differences and train patients appropriately [9, 10].

In the past, innovations in pump therapy were primarily cosmetic (e.g., availability in multiple colors and accessories). Insulin pumps are now following the lead of consumer electronics and have introduced features such as color touch screens, USB-rechargeable batteries, single used insulin cartridges, and disposability. The availability of multiple infusion set types, various catheter tubing lengths, and tubeless pumps (where the infusion set and reservoir are integrated) have enhanced the acceptability of pump therapy and led to increased pump usage [9, 10, 11]. For many years, insulin pumps have received data transmitted from glucose meters. Insulin pumps can now display data from a continuous glucose sensors on the same screen and share data for display on other remote devices. This feature is likely to become more common in the next few years. However, currently most require a computer connection [4, 9, 11].

The following insulin pump models are currently available: Animas 2020 (Animas, Johnson & Johnson), Paradigm real-Time mmT-522 (Medtronic), Paradigm real-Time mmT-722 (Medtronic), Dana Diabecare (Sooil), Accu-Chek Spirit (Roche Diagnostics), Accu-Chek D-Tron Plus (Roche Diagnostics) and Deltec Cozmo (Smiths Medical).

Continuous subcutaneous insulin infusion therapy makes use of an external pump that delivers insulin continuously from a refillable storage reservoir by means of a subcutaneously placed cannula. The pump can be programmed to deliver a basal rate of insulin throughout the day, with higher infusion rates triggered by the push of a button at meal times. This may be a bolus or over a period of time, and it can also deliver different basal rates of insulin at different times of the day and night. It is recommended that the cannula is replaced and repositioned every 3 days. Specific complications of continuous subcutaneous insulin infusion therapy include reactions and occasionally infections at the cannula site, tube blockage and pump malfunction [7, 8, 12].

Continuous subcutaneous insulin infusion or insulin pump therapy is recommended to type 1 and insulin-requiring type 2 with [4, 6, 13, 14]:

- elevated HbA1C;
- glycemic variability;
- recurrent hypoglycemia, nocturnal hypoglycemia, activity-induced hypoglycemia and hypoglycemia unawareness;
- pregnancy/pre-pregnancy;
- recurrent diabetic ketoacidosis/recurrent hospitalizations;
- «dawn phenomenon»;
- gastroparesis;
- patient preference, meal-timing flexibility and normalization of lifestyle;
- low insulin requirements (not easily measured via syringe) (Table 1).

**Table 1:** The clinical characteristics of patients for pump insulin therapy (adapted from American Association of Clinical Endocrinologists/ American College of Endocrinology, 2014).

Diabetes mellitus type 1	Diabetes mellitus type 2
<p>Patients with type 1 diabetes mellitus who do not reach glycemic goals despite adherence to maximum multiple daily injections, especially if they have:</p> <ul style="list-style-type: none"> <li>• very labile diabetes (erratic and wide glycemic; excursions, including recurrent diabetic ketoacidosis);</li> <li>• frequent severe hypoglycemia and/or hypoglycemia unawareness;</li> <li>• significant “dawn phenomenon,” extreme insulin sensitivity.</li> </ul> <p>Special populations (e.g., preconception, pregnancy, children, adolescents, competitive athletes).</p> <p>Patients with type 1 diabetes mellitus who, after investigation and careful consideration, feel that CSII would be helpful in achieving and maintaining treatment targets and improve their ability to cope with the challenges of managing their diabetes.</p>	<p>Selected patients with insulin-requiring type 2 diabetes mellitus who satisfy any or all of the following:</p> <ul style="list-style-type: none"> <li>• C-peptide positive, but with suboptimal control on a maximal program of basal/bolus injections (Note: CMS will not reimburse for pumps or pump supplies in type 2 diabetes mellitus patients who are not C-peptide deficient);</li> <li>• substantial “dawn phenomenon”;</li> <li>• erratic lifestyle (e.g., frequent long-distance travel, shift work, unpredictable schedules leading to difficulty maintaining meal timing);</li> <li>• severe insulin resistance.</li> </ul> <p>Selected patients with other DM types (e.g., postpancreatectomy).</p>

The paediatric clinical specialist emphasised the difficulty in controlling blood glucose in very young children because of their sensitivity to insulin, small size and irregular lifestyle, and noted the special relevance of insulin pumps to this age group. The time of puberty was also identified as a difficult time to control diabetes because of hormonal and psychosocial reasons. Insulin pump therapy would be recommended as a possible treatment for these patients if treatment with multiple daily injections is not practical or is not considered appropriate. In patients with poorly controlled type 2 diabetes despite using multiple daily injections of insulin, pump treatment can be considered as a safe and valuable treatment option [3, 14-16].

Patient requirement for continuous subcutaneous insulin infusion: responsible and psychologically stable, willingness to monitor blood glucose a minimum of 2-3 times a day, willingness to quantify food intake, willingness to comply with medical follow-up [6, 15, 18]. Insulin pump therapy should only be started by a trained specialist team. This team should include a doctor who specialises in insulin pump therapy, a diabetes nurse and a dietitian (someone who can give specialist advice on diet) [18, 19]. This team should provide structured education programmes and advice on diet, lifestyle and exercise that is suitable for people using insulin pumps. Insulin pump therapy should only be continued if there has been a sustained improvement in the control of their blood glucose levels. Such goals should be set by the doctor through discussion with the person or their carer [5, 8].

The patient or guardian: is responsible for ensuring the correct operation of the insulin pump will rotate the infusion set consistent with the recommendations for the device. This will be every three days, unless other documentation is provided will make the adjustments to the insulin pump program will be responsible for all bolus dose administration. If the patient is not capable of under taking the seactions, the insulin pump must be discontinued [7, 8].

The insulin pump may need to be discontinued temporarily during a number of circumstances during hospitalisation. In this situation, discontinuation of the insulin pump for more than 30 minutes may result in significant hyperglycemia. Such circumstances where the insulin pump needs to be temporarily disconnected include: any radiological investigation (pump must be removed), CT scan (pump must be removed), MRI scan (pump must be removed, including metal cannula), physiotherapy (depending on the therapy), hydrotherapy (even if the pump is labelled as water-proof).

Patients whose insulin pump needs to be discontinued for longer than one hour may need to be considered for an injection of subcutaneous insulin, eg subcutaneous soluble insulin (Actrapid, Humulin R, Humalog, Novorapid or Apidra) to cover their short term requirements. Alternatively, the pump can be discontinued for up to two hours at the discretion of the treating doctor if the patient is clinically stable and blood glucose levels are being monitored regularly. Upon recommencement of the pump, blood glucose should be rechecked and if needed a correction bolus can be given [7, 8, 11].

For the first time, in 2010 the Cochrane Database System review compared continuous subcutaneous insulin infusion use with multiple daily injection insulin regimens [12]. This review included 23 randomized studies (duration, 6 days to 4 years) involving 976 patients with diabetes mellitus type 1. A significant difference was documented in HbA1c response favoring insulin pump therapy (the HbA1c decrease after starting continuous subcutaneous insulin infusion therapy was in the range 0.2–1.6%). In addition, insulin pump therapy users demonstrated greater improvements in quality of life measures. No difference in body weight was observed between the both treatments. Severe hypoglycemia appeared to be reduced in continuous subcutaneous insulin infusion users [7, 8, 17]. The trials in type 1 diabetes mellitus in children and adolescents reported a statistically significant greater reduction in HbA1c levels following 16 weeks of continuous subcutaneous insulin infusion compared with analogue-based multiple daily injections therapy. There were statistically significant fewer episodes of severe hypoglycemia, ketoacidosis, and reduction in daily insulin dose also. There was no evidence of a statistically significant difference in glucose variability or weight between the two groups [16]. The six observational studies of continuous subcutaneous insulin infusion therapy in pregnant women with type 1 diabetes mellitus were studied. They showed statistically significant lower HbA1c levels in women on continuous subcutaneous insulin infusion compared with multiple daily injections therapy [4, 7].

**Conclusion**

The use of continuous subcutaneous insulin infusion therapy improved glycemic control and decreased glycemic variability, improved control of «dawn phenomenon», decreased severity and frequency of hypoglycemia. The insulin pump therapy increased flexibility, normalization of

lifestyle and sense of well-being in patients with both types of diabetes mellitus. The perspectives of future investigations. Beyond improvements in the pump-user interface, there is a clear need for educational programs administered by qualified physicians to provide patients with initial and follow-up pump use. Research continues toward a fully closed-loop “artificial pancreas” that will integrate continuous glucose monitoring and insulin pumps that doses the correct amount of insulin at the right time with the ultimate goal of normalizing glucose levels automatically. Another expected stage is a system that will automatically administer or withhold insulin if glucose levels pass beyond set limits. It is clear that even after more than 3 decades of clinical insulin pump use in medical practice, many critical questions remain.

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