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Review Article

APPLICATION OF INSULIN PUMP IN THE TREATMENT OF DIABETES MELLITUS

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ABSTRACT

Continuous subcutaneous insulin or the insulin pump has gained the popularity and sophistication as a near-physiologic programmable method of insulin delivery that is flexible and lifestyle-friendly. Insulin pump therapy is mainly used for people with type 1 diabetes and those with type 2 diabetes with increased insulin requirements. Insulin pump used provides a near physiological basal bolus insulin delivery method that, in theory, mimics normal pancreatic function better than injection. Although insulin pump therapy increases quality of life and decreases complications related diabetes but it requires increase frequency of blood glucose monitoring, and it may have complicated by infusion site infection and diabetic ketoacidosis.

Key words: Diabetes Mellitus; Insulin pump; Safety; Validity

INTRODUCTION

Diabetes is rapidly becoming a major health epidemic in most regions of the world[1].All the patients with type 1 diabetes mellitus and a significant number with type 2 diabetes mellitus requires the use of insulin for controlling blood glucose. In the last 20 years, technological innovation and bioengineering has transformed the diabetes landscape. There are several varieties of insulin and many different injections regimes that can be used. However, in spite of the availability of insulin vials and pens, the acceptability for the patients and the glucose reading that are obtained with the use of single or multiple dose injection regimens is not to the desired level. Insulin pump therapy also known as continuous subcutaneous insulin infusion (CSII). However even modern infusion pump errors of insulin infusion can occurs due to pump failure, insulin infusion set(IIS) blockage, infusion site problem, infusion instability issue, user error, or a combination of these.

Figure 1: Insulin pump therapy is a method of administration that more closely resembles physiological delivery and is increasingly utilized treatment for selected patients with type 1 diabetics as a means of achieving improved glycaemic control.

Users are therefore exposed to significant and potentially fatal hazards. Control of diabetes is monitored by measuring glycosylated hemoglobin (HbA1c). We know that achieving optimal control of diabetes reduces the development of diabetes related complications such as renal failure and blindness. Optimal control is difficult to achieve and although some people will manage this with MDI, other will not, and insulin pump therapy pump may present as an alternative option [2]. Insulin pump therapy or continuous subcutaneous insulin infusion(CSII) is a method of insulin delivery that is more closely resembles physiological insulin delivery [3]. It is an increasingly utilized treatment for selected patient with type 1 diabetes as means of achieving improved glycaemic control[4].

How do insulin pumps work?

Insulin pump delivers insulin by continuous infusion through a single subcutaneous site which is replaced, on average, every 3 days. Only rapid acting insulin is used, and the analogue insulin's have gained popularity over regular insulin for this purpose [5]. Insulin deliver via the pump through a cannula inserted subcutaneously. The cannula remains in situ for up to 72 hours and must be changed. Patients who go on to insulin pumps are trained in the calculation of insulin dosing using carbohydrate counting. This is the process where a patient "counts " how much carbohydrate is contained in the food they are eating, and calculates the insulin required for this meal. All foods containing carbohydrate will have an effect on blood sugar so need to be covered with the additional insulin dose, known as the bolus dose. At every meal the carbohydrate count is entered into the pump to give an additional dose of insulin. All of the commercially available pumps are "smart pump" so they contained on board calculator that will calculate the amount of insulin required for any given carbohydrate value and also suggest a correction dose to restore the blood glucose back to the normal range if it is outside of this prior to eating. When the patient checks their finger-prick blood glucose this information is transmitted via Bluetooth to the pump. Smart calculators reduced the complexity for patient and allow finer adjustment for insulin for a given carbohydrate load [3]. Insulin is delivered by the pump in two ways: (a) as a basal insulin or insulin that is delivered at programmed rates throughout the entire day to match the individual's base-line insulin requirements, or (b) as a bolus that provides an additional boost of insulin to cover for the ingested carbohydrates or elevated blood glucose levels. The amount of insulin bolus is calculated using the pump and is managed by the patient [6]. Rapid acting insulin including lispro, asparte, and glulysin,is the recommended insulin for the pump therapy because of improved absorption profiles[7]. Amount of insulin as small as 0.025 units are delivered into the subcutaneous tissue from the pump through small tubing called a cannula. The insulin is then absorbed from the subcutaneous tissue at smaller rates as when injected by syringe or pen. Additionally, insulin pumps have multiple functions to offer advantages to patient who exercise. The basal rate can be increased or decreased by a set percentage before, during or after exercise. There have been number of advances in insulin pump therapies. Patch pumps or tubeless pumps consists of patch(reservoir of insulin and tiny pump) attached to the skin with the smart calculator and glucose monitor as a separate hand hold device communicating by Bluetooth. This has the advantage of no long wires communicating the pump to the patients. The technologies to assist patient in managing their diabetes are progressing rapidly with the potential to end blood glucose monitoring, by using devices that measure the interstitial glucose in a semi-continuous manner and communicate directly with the pump[8].

Pros of insulin pump therapy	Cons of insulin pump therapy
Cost effective in terms of quality-adjusted life-years (QALYs).	Cost between £2000-3000.
Increased flexibility in life style.	Not all patients want to attachto machines 24 hours per day.
Increased freedom with food.	Psychological body image barriers, particularly teenagers.
Reduced hypoglycemia and glucose variability.	Concern over pump failure
Possible 30-40 % insulin dose reduction on initiation may help weight loss.	Requires increased frequency of blood glucose monitoring
Assist in case of severe needle phobia	Not always easy to change the infusion set.
Benefits those with lipohypotrophy and/or lipoatrophy.	Perceived increased risk of diabetic ketoacidosis among some patients.

Table 1: Pros and cons of insulin pump therapy [9-11].

Evolution of the insulin pump technology:

The first insulin pumps where bulky machines that were employed only for research purposes. Pumps were commercialized for use in the general diabetic patient population in 1970s. They required patients to calculate the amount of bolus insulin for food coverage and for high glucose reading[13]. Technological capabilities have advanced dramatically since that time, and pump use has increased manifold. Statistics shows that an estimated 350,000 people in United States (US) use insulin pumps today and about 30,000 of those believed to have type 2 diabetes[14]. Rate of CSII use appear to vary greatly internationally[15, 16]. The total number of pump users worldwide is unknown as the numbers sold and operating are not currently reported by the manufactures but, estimates from financial reports suggest that the number may be 0.75-1 .0 million. A recent Medtronic MiniMade Paradigm and 530 G pump recall included 444, 374 units in US and 293,000 patients elsewhere [17]. Nowadays available pump deliver basal insulin in increments of as little as 0.01 units per hour, and use automatic bolus insulin calculators. Although the pump and its supplies (insulin cartridges, tubing, and infusion sets) remains expensive, insurance coverage has improved considerably over the years with phenomenal advances in self monitoring of blood glucose, meters are able to communicate the reading directly and wirelessly to pump via infrared technology thus eliminating the extra step of manual entry of the glucose value into the pump by the patients. Touch screen technology and user-friendliness have been incorporated on average, and insulin pump cost about US $ 6000 and supplies between US $ 3000 and $ 6000 annually. Patients who switch from multiple-dose insulin injection(MDII) to pump in a managed care setting realize a reduction in insulin expenditures of around US $ 657 per year [18].

Figure 2: The T-slim insulin pump is popular with young patients due to its new touch-screen.

Figure 3: The OmniPod tubeless insulin pump with a pod(right) and hand held device that functions as a blood glucose meter and communicates wirelessly with the pod to deliver insulin based on the patient's personal settings.

Potential advantages of pump therapy:

The expected benefits of insulin pump therapy are summarized in table. Insulin pump use provides a near physiological basal bolus insulin delivery method that, in theory, mimics normal pancreatic function better than injection[19]. Precise insulin dosages can be programmed and administered, giving the patient increased flexibility in daily living with regard to meal times, travel work schedule etc.[20]. Observational studies, meta-analysis and randomized clinical trials have demonstrated improvements in long-term glycaemic control when compared with daily multiple dose insulin injection[21-23]. Evidence from clinical studies suggests that pump therapy is associated with the decreased riskof hypoglycemia and the need for emergent medical care [24]. The later translates into reduction in the cost of care and utilization of health care resources [25]. Quality of life measures have shown improvement with pump therapy compared with MDII [26]. One clear advantage that pump therapy provides in the decreased number of syringe needle sticks that are required [7]. Pump therapy also reduces in need for hospitalization; improve quality of life and treatment satisfaction.

Problematic hypoglycemia:

Many patients with type 1 diabetes will struggle with persistently elevated Hba1c levels. Current guidelines recommended an Hba1c is between 48 and 58mmol/mol [2]. Aiming for tight glycaemic control may result increased frequency of hypoglycemia. Severe hypoglycemia (requiring third party assistance) may occur up to 40 % of patients with type 1 diabetes [27]. Insulin pump therapy may allow reduce glucose variability, which can reduce the risk of hypoglycemia and, therefore, increase confidence to improve overall control[27].

Persistence suboptimal diabetes control:

Initiation of insulin pump therapy on average leads to a reduction in Hba1c of between 3.3 and 6.6 mmol/mol. The greatest reduction in Hba1c is seen in those patients with a higher Hba1c at baseline [28]. NICE advices insulin pump therapy for a patient with Hba1c above 69 mmol/mol. This is the level at which insulin therapy is the most cost-effective in terms of improvement in quality – adjusted life years [12, 27].

Children and type 1 diabetes:

In pediatric care thresholds for insulin pump therapy are lower because many pediatricians see multiple daily injections of insulin as being impractical for children. This is supported by NICE for children under 12 years, although those over 12 should be treated with same guidelines as adults [12]. Many pediatric centers in UK now use insulin pump therapy as first-line treatment upon diagnosis of type 1 diabetes [27, 40].

Pregnancy and insulin pump therapy:

Tight glucose control is advised at the time of conception and pregnancy to reduce pregnancy related complications. Insulin pump therapy in pregnancy can help patients achieve optimal control. Any reduction in HbA1c before and sustained during pregnancy increase the chance of a successful pregnancy. The risk of hypoglycemiacan be increased because of the intensive regimen to improve glycaemic control. Insulin pump therapy can reduce the episodes in pregnant patients.

Insulin pump therapy in type 2 diabetes mellitus:

The evidence for CSII in type 2 diabetes remains limited [7, 29, 30-32, 36]. In Raskin et al.'s study of patients with type 2 diabetes; CSII and multiple daily injections were found to be equally efficious and safe, but 93 percent of CSII users expressed a preference for CSII compared with their previous regimen of multiple daily injections [31]. Harman et al. compared CSII with multiple daily injections in a sample of patients aged 60 or older with type 2 diabetes; efficacy, rates of hypoglycemia and weight gain were similar in the 2 modalities [36]. A study by Wainstein et al. focused on CSII in sample in obese patient with type 2 diabetes and found improvement in A1c over multiple daily injections without significant changes in weight, although goal A1c

levels were not attended [32]. These studies suggest that CSII should be considered for type 2 diabetes patients requiring intensive insulin therapy, [33,34] but more studies are needed.

Potential Disadvantage of Insulin Pump Therapy:

Remembering to bolus:

Giving an insulin bolus with each meal or snack that is greater than 5 gm of carbohydrate is difficult for some people to remember. Hba1c values will not improved if boluses are forgotten and fact they may rise. If the bolus is forgotten, the blood sugar will rise quite high.

Ketouria or ketoacidosis:

Because the insulin pump delivers only very small subcutaneous amount of insulin analogues with a short activity life, there is an increased risk for developing diabetic ketoacidosis (DKA) if insulin deliver is interrupted. Because of this risk, it is important that the patients self- monitor blood glucose frequently throughout the day,[29, 35] thus patients using insulin pumps may require as many finger sticks as patients using multiple daily insulin injections[29]. Fortunately, it has been shown that the rate of DKA with pumps has been reduced with proper pump education and management [32].

Skin infections and local site infection:

The most common complication of pump therapy are infusion site irritation, occlusion, or, occasionally, infection [29]. Infection can occur at the local sites particularly, if the infusion sets are left in for longer than 3 days. If redness, heat, and/or pus are noted at insertion, such area should not be used again as an infusion site until it has healed.

Psychological Factors:

CSII is a complex mode of insulin delivery when considering patient ease of use [7]. Patients under consideration as candidates for CSII should be evaluated closely to determine if they are capable and motivated to learn CSII techniques, which include, carbohydrate counting and frequent self monitoring [35]. CSII is discouraged for patients who have a history of non compliance with self monitory or current insulin regimens significant psychological problems, or learning disabilities [32, 35]. Adherence to blood glucose self monitoring and the ability and willingness to regularly communicate with the professional pump team is absolutely critical in predicting long term success with the pump [38].

Expenses:

Although pumps are expensive it may prevent from eye, kidney and nerve complications of diabetes if the Hba1c level improves. On average, an insulin pump costs about US$ 6000 and supplies between US$ 3000 and $ 6000 annually. Patient who switches from multiple-dose insulin injections (MDII) to pump in a managed care setting realized a reduction in insulin expenditures of around US$ 657 per year [18]. The benefit afforded by integrated pump- sensor technology should also be weighed against its complexity and cost [39].

Insulin unavailability and storage:

Insulin may not be available on time. Insulin spoils if it fridge or reaches temp above 90°F.

Indication for insulin pump treatment:

The ideal candidate for initiation for insulin pump therapy is a motivated patient who is knowledgeable in the important aspects of diabetes self-care and desires better glycaemiccontrol [37].

- Suboptimal glycaemic control in spite of efforts multiple daily insulin injections.
- Frequent or unpredictable hypoglycemia unawareness.
- “Dawn” phenomenon with persistent early morning hypoglycemia.
- An active life style (exercise, strenuous physical activity, athletic pursuits).
- Children and young adults who typically desire fewer restrictions and more flexibility.
- Growth spurt of adolescence.
- Preconception planning and pregnancy.
- Presence of gastroparesis.
- Hectic life style and frequent travel.
- Shift work and erratic daily schedules.
- Need for flexibility in amount and timing of meals.
- Type 2 diabetes with increase insulin requirements.

CONCLUSION

Insulin pump therapy is an increasingly used method for managing type 1 diabetes and those type 2 diabetes with increased insulin requirement. Although this therapy is expensive, it has demonstrated improvement in quality of life by improving Hba1c level and preventing from diabetic related complications like diabetic retinopathy, diabetic nephropathy and diabetic peripheral neuropathy etc.

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