Insulin pump therapy in type 1 diabetes: advantages and disadvantages

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Abstract — The current goals for the therapy of children and adolescents with type 1 diabetes mellitus are to achieve as near-normal glycaemia with a minimum risk of severe hypoglycemia, to limit excessive weight gain while achieving adequate growth, to improve quality of life for both the patients and their families, and to delay or prevent vascular complications. Insulin pump therapy provides a treatment option that can significantly aid in achieving all of these goals. It can provide greater flexibility in the timing of meals and snacks, has programmable basal rates to optimize overnight glycemic control, can reduce the risk of exercise-induced hypoglycemia, and enhances the ability of the patient and the family members to achieve acceptable diabetes control. The aim of this analysis is to evaluate the advantages and disadvantages of insulin pump therapy in children and adolescents with type 1 diabetes. Since August 2002, 18 children and adolescents with type 1 diabetes have been switched from multiple daily insulin injections to insulin pump therapy. Insulin pumps used were 9 - Medtronic Minimed 508, 6 - Medtronic Paradigm and 2 - Accu-Chek Spirit. The reasons for initiating insulin pumps were: frequent episodes of hypoglycaemia, “dawn” phenomenon, brittle diabetes, insulin resistance. Another 2 type 1 diabetic women have been switched during pregnancy to insulin pump. The duration of insulin pump therapy was 25.3 ± 15.9 months. The initial mean value of HbA1c was 8.35 ± 1.3 %, the subsequent mean values were 7.9 ± 1.3 % and 7.6 ± 1.1 %. The quality of life has improved significantly for both parents and children. The 2 pregnant women had a significant improvement of glycemic profile and HbA1c. No severe episodes of hypoglycemia have been recorded. Insulin pump is a modern tool for insulin therapy with proved advantages over intensive insulin therapy with multiple daily injections.

Keywords: insulin pump therapy, glycemic control.

1. INTRODUCTION

The modern medicine paradigm implies an intensive, safe and treat-to-target clinical management, based on evidence resulted from clinical trials. The main goal of the therapy in type 1 diabetes, is to achieve the glycemic control. Extended goals are to achieve as near-normal glycaemia as possible, with a minimum risk of severe hypoglycemia, to limit excessive weight gain, to delay or prevent chronic complications and to improve patient quality of life. There is now a great body of evidence that an intensive insulin treatment combined with glucose self-monitoring, aiming to achieve near-normal levels of glycated hemoglobin A1c (HbA1c), is a surrogate marker of glycemic control, is associated with a significant lower risk of late complications. Prospective, randomized, clinical trials in type 1 diabetes such as the Diabetes Control and Complications Trial (DCCT), have shown that improved glycemic control is associated with sustained decreased rates of microvascular (retinopathy and nephropathy), macrovascular, and neuropathic complications. An increase of HbA1c above 7.5% (or more than approximately 120% above the upper level of the normal reference range), is associated with a significantly increase in the risk of later microvascular complications. [1-4] The American Diabetes Association consensus statement considers that HbA1c, goal for patients in general is bellow 7%. [5] Due to specific conditions related to the diabetes treatment in children and adolescents, the International Society for Pediatric and Adolescent Diabetes (ISPAD) stated that for each individual the target should be the lowest achievable HbA1c without the occurrence of frequent or severe hypoglycemia. [6] Glycaemic targets are presented in Table 1.

In children and adolescents with type 1 diabetes, achieving adequate growth, safe treatment and quality of life for both patients and their families, is extremely important. Multiple daily insulin injections, in a basal-bolus regimen are considered now the most physiologic insulin treatment in type 1 diabetes. Diabetes mellitus is a field where new technologies are very important and extremely useful to ensure a long-term successful therapy. Starting with glucometers which allow frequent self-monitoring of blood glucose, new medical technology, such as insulin pumps and continuous glucose monitoring systems, is more and more proved to be useful tools for a better therapy. In DCCT, the patient group intensively treated succeeded a HbA1c reduction of 1.7 %. In the last year of the trial 42% of patients were using insulin pump, which has been associated with a further 0.2% - 0.4% reduction of HbA1c, along with an increase in lifestyle flexibility. [7,8]
Achieving optimal blood glucose control is especially challenging in younger patients with type 1 diabetes. Inadequate glucose control can lead to wide glycemic excursions or frequent hypoglycemia. Recurrent episodes of hypoglycemia at a very young age have been associated with neurocognitive dysfunction. Fear of hypoglycemia is prevalent in adolescents and families of children with type 1 diabetes and may pose a barrier to improved glycemic control. Insulin pump therapy, due to continuous subcutaneous insulin infusion (CSII), provides a modern treatment option that can significantly aid in achieving the therapeutic targets while reducing the hypoglycemia and improving the quality of life. CSII is the most physiologic method of insulin delivery currently available. It is able to closely simulate the normal pattern of continuous insulin secretion, the 24-hour basal rate, upon which prandial “boluses” are superimposed. Continuous subcutaneous insulin infusion therapy has become an increasingly used, effective, safe treatment in children and adolescents with type 1 diabetes. [9-11]. Number of children treated with CSII is continuously growing. [12] CSII has been demonstrated to effectively reduce hypoglycemia, while ketoacidotic events are not increased. [11,13] Compared with multiple daily injections, CSII allows for higher flexibility in timing meals and snacks, which is of particular importance in young children with often unpredictable food intake, enabling intensive treatment with painless insulin delivery. In addition, CSII provides the unique opportunity to adapt the hourly basal insulin infusion rate to different patterns of insulin requirements, according to sex-, age-, and puberty-related changes in their endocrine system, reflecting individual circadian distribution of basal insulin needs. Seven patterns of basal insulin profiles have been found in children and adolescents. [14]

**The advantages** associated with insulin pump therapy are now recognized in terms of metabolic control, psychological impact and quality of life. [15-17]

**Metabolic advantages** refers to:
- Better simulation of the beta-cell function,
- Better insulin pharmacokynetics,
- Constant and reproducible subcutaneous insulin absorption, leading to reduced glycemic fluctuations and reduced risk for hypos,
- Programmable basal rates that can individualize the insulin dose delivery and consequently optimize overnight glycemic control and “dawn” phenomenon,
- Programmable several patterns of basal rate can adjust the insulin regimen according to different conditions the patient can be (sports, intercurrent illnesses),
- Low insulin doses when required (children, renal impairment),
- Reduced risk of exercise-induced hypoglycemia,
- Better adherence to correction of hyperglycaemia with additional boluses.

Comprehensive studies that have compared the efficiency in glucose control with insulin pumps versus multiple daily injections, have demonstrated either similar results, or superior results with pumps, but the frequency and the duration of hypoglycaemic episodes are reduced with insulin pumps.

**Advantages related to lifestyle:**
- Greater flexibility in lifestyle, in terms of work, meals, physical activity
- Greater flexibility in the timing of meals and snacks. The 3 types of boluses, normal, dual, square, can provide a better postprandial glycemic control due to a more precise adaptation to the carbohydrates content of the meal. The “wizard” bolus, available in Medtronic Paradigm pump, calculates the amount of insulin, taking into account the actual glycemic value, the glycemic target (set before), the content of carbohydrates in the meal, the insulin sensitivity factor and the active insulin remained from the previous bolus.

**Psycho-emotional impact:**
- Increased adherence and satisfaction with the treatment
- Improved quality of life of both children and their parents.

The recent international statement, considers the indications for CSII as follows: [16]
- Recurrent severe hypoglycemia
- Wide fluctuations in blood glucose levels regardless of HbA1c
- Suboptimal diabetes control
- Microvascular complications and/or risk factors for macrovascular complications
- Good metabolic control but insulin regimen that compromises lifestyle

Other circumstances in which CSII may be beneficial include:
- Young children and especially infants and neonates
- Adolescents with eating disorders
- Children and adolescents with a pronounced

<table>
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<th>Suboptimal</th>
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<td>&lt; 3 or &gt; 9</td>
<td>&gt; 11</td>
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<td>&lt; 7.6</td>
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**Table 1. Glycaemic targets in Type 1 Diabetes** [6]
OBJECTIVE

The aim of this analysis is to evaluate the advantages and disadvantages of insulin pump therapy in children and adolescents with type 1 diabetes, based on the clinical experience accumulated in this field by the medical team from the Clinical Center of Diabetes, Nutrition, Metabolic diseases, Cluj-Napoca, Romania.

3. Studied group and methods

Since August 2002, 18 children and adolescents with type 1 diabetes have been switched from multiple daily insulin injections to insulin pump therapy. Mean age is 15.9 ± 5.6 years, the youngest has 6 years and the oldest 32 years. The mean duration of diabetes when started the insulin pump therapy was 12.8 ± 6 years, minim 5 year and maxim 27 years. The reasons for initiating insulin pumps were: frequent episodes of hypoglycaemia, “dawn” phenomenon, brittle diabetes, insulin resistance. As a temporary insulin pump therapy, 2 pregnant women with type 1 diabetes have been switched to pump in the third month of gestation, due to an augmented “dawn” phenomenon in one case and frequent hypoglycaemia in the other case. Insulin pumps used are Medtronic MiniMed 508 in 10 patients, Medtronic Paradigm 712 in 4 patients, Medtronic MiniMed Paradigm 722 Real Time in 2 persons, and Accu-Chek Spirit in 2 persons. A special mention should be made regarding the new MiniMed Paradigm 722 Real-Time, which is the world's only system to integrate an insulin pump with REAL-Time continuous glucose monitoring. The advantages of this system are that it displays glucose readings every five minutes, offers safety alarms, and displays 3- and 24-hour trend data that help proactively intervene to improve glucose control, and reduce the severity and duration of low and high blood sugars.

RESULTS

Mean duration of insulin pump therapy is 28.9 ± 15.8 months. Overall, the initial mean value of HbA1c was 8.35 ± 1.3 %, the subsequent mean values were 7.9 ± 1.3 % and 7.6 ± 1.1 %. In 11 patients, the glycaemic control has been significantly improved, from the initial HbA1c of 8.76 % ± 1.8 to 7.2 ± 0.7 (p < 0.01). An example of the glycaemic profile achieved by insulin pump and monitored by continuous glucose monitoring system, is displayed in Figure 1. The corresponding basal rate is displayed in Figure 2. Three of the young patients have a suboptimal HbA1c, probably due to the onset of puberty when glycaemic control is more difficult. Four patients remain in the optimal area of glycaemic control, but with less hypoglycaemia and glucose variability then before insulin pump. The two pregnant women had a significant improvement of glycaemic profile, from HbA1c of 8.4 % to 6.4 % and from 7.8 % to 6.7 %. No severe episodes of hypoglycaemia have been recorded. The flexibility of lifestyle has been significantly improved: two of the children are involved in regular sport activity, meal schedule and content are more easily adapted to the school program, the low frequency of hypoglycaemia allows children to be more independent and parents more confident. Overall there is a unanimous agreement that quality of life has improved significantly for both parents and children.

Figure 1. Glycaemic profile in insulin pump therapy
5. CONCLUSION

Insulin pump is a modern tool for insulin therapy with proved advantages over intensive insulin therapy with multiple daily injections. Major benefits are achieved when insulin pump therapy is associated with patient motivation and commitment to achieve glycaemic control and with blood glucose self-monitoring.

6. REFERENCES

[16] Moshe Ph., Battelino T., Rodriguez H., Danne Th., Kaufman F., for the consensus forum participants. Use of Insulin Pump Therapy in the Pediatric Age-Group Consensus statement from the European Society for Paediatric Endocrinology, the Lawson Wilkins Pediatric Endocrine Society, and the International Society for Pediatric and Adolescent Diabetes, endorsed by the American Diabetes Association and the European Association for the Study of Diabetes, Diabetes Care, vol. 30 (6), pp. 1653, 2007