METABOLIC CONTROL OF TYPE 1 DIABETES IN CHILDREN TREATED WITH INSULIN PUMP THERAPY

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Abstract

In this paper we present study of metabolic control in children suffering from TYPE 1 Diabetes Mellitus (T1DM) who use insulin pump (IP) therapy, and who were treated at Paediatric Clinic in Sarajevo.

In retrospective study we followed all T1DM patients with IP therapy introduced in the period from 1st March 2005 to 1st September 2008.

We analyzed their age and sex structure, therapy before IP use, and the metabolic control of T1DM represented with glycosylated haemoglobin (HbA1c) value just before and 6 months after IP therapy introducing.

The total number of observed patients was 39. There were 24 boys (61,5 %) and 15 girls (38,5 %) with the age range between 12,3 ± 3,2 years. Most patients were from age group 8-14 years. In the same number of patients 17 (43,6 %) diabetes duration was less than 5 years and 5-10 years. Before IP introduction most patient 61,5 % use therapy with insulin analogues. Mean value of HbA1c before IP therapy introduction was 8,57±1,65 % and 6 months after IP therapy introduction HbA1c 7,53 ± 0,81 % (p = 0,0009). There was significant reduction HbA1c values even 6 month after IP therapy introduced.

Therapy with IP in children with diabetes was very efficient in achieving therapeutic goal of T1DM treatment (HbA1c<7,0 %) what will protect patients from appearance and progression of chronic micro vascular complications on eyes, kidneys and peripheral nerves.

KEY WORDS: TYPE 1 Diabetes Mellitus, insulin pump, glycosylated haemoglobin, children

Introduction

TYPE 1 Diabetes Mellitus (T1DM) is the most frequent endocrinologic disease in children. Chronic course of the disease, and life-long substitution insulin-therapy which must be coordinated with the food, physical activity and with the results of self-monitoring blood glucose are the factors that make life of these children and their families very difficult. Bad metabolic control of T1DM that is represented with glycosylated haemoglobin level (HbA1c) higher than 7,0 % leads to chronic micro vascular complications: nephropathy, retinopathy and neuropathy. Progression of chronic complication in the patients with long-lasted bad metabolic control of diabetes results in invalidity and lethal outcome (1). The aim of the treatment of diabetes is achievement of long-lasting good metabolic control of the illness with HbA1c level less than 7,0 %. DCCT study documented that decrease of HbA1c for 10,0 % reduces incidence of chronic diabetes complication for 43-45 % (2). Each kind of therapy that can provide attaining of this aim parallel with normal growth and development of the child is justified. Increasing use of insulin pumps (IP) in therapy of diabetes characterized last decade. This therapy is the most similar to physiologic way of insulin secretion in non-diabetic persons because it is 24-hours lasting subcutaneous delivery of insulin (basal delivery) with bolus dose delivery in the meal-time (3). Numerous studies confirmed that patients with IP therapy reach better metabolic control of their T1DM with less hypoglycaemic episodes and stabile body weight (4, 5). Less number of injections for 10-15 times during IP therapy compared to intensive insulin therapy (4 insulin doses daily), is very important for patient. Instead of prick with needle for every dose of insulin in IP therapy insulin is continuously delivered through thin, small plastic tube subcutaneously positioned which is replaced every 3-4 days. All these technical preferences of IP therapy enable more flexibility in time and quality of meals that significantly improves life quality of young patient and his family (6). Although the price of IP therapy is significantly higher than for intensive insulin therapy, long-lasting positive effects of this therapy in children excuse their use. (3, 7) IP therapy was introduced for the first time in Bosnia and Herzegovina at Paediatric Clinic of University of Sarajevo Clinics Centre for T1DM patients in 2005 year. Patients for IP therapy were selected according medical and non-medical indications that were established on the base of indications from leading Diabetes Associations and authors. Those indications were originally fitted to our needs (8, 9). Our indications for introducing IP therapy were: medical and others. Medical indications were: bad metabolic control of T1DM (HbA1c> 8,0%), significantly elevated insulin autoantibody (>15,0), early age of T1DM beginning (age< 7 years), duration of T1DM (≥ 5 years) and associated diseases. Other indications were: motivation for IP therapy, T1DM in closest relative and bad life quality during previous treatment. Patients had to satisfy at least one indication from each group. Leading indications for IP introducing were significantly elevated insulin autoantibody, motivation for IP therapy and bad life quality. All patients satisfied at least 4 indications.

Aim of the Study

The aim of this study is to correlate the level of metabolic regulation represented with HbA1c value in children and adolescents with T1DM before and 6 months after introduction of IP therapy. Patients were treated at Paediatric Clinic in Sarajevo.

Material and Methods

All patients 0-18 years of age suffering from T1DM and treated with IP therapy at Paediatric Clinic in Sarajevo were observed in this study. This study represents retrospective analysis of metabolic control of children suffering from T1DM in who was introduced IP insulin therapy in the period from the 1st March 2005 to the 1st September 2008.

We analysed:

- patients according sex and age
- duration of T1DM
- therapy before IP introduction
- HbA1c value just before IP therapy introduction
- HbA1c value 6 months after IP therapy introduction

Data were collected from patients' histories. T1DM was diagnosed and treated at Paediatric Clinic in Sarajevo. Data concerning insulin therapy were updated at least every three months at check-up time. All patients had insulin pumps produced by Medtronic Minimed and models were 508 and 712. HbA1c estimation was performed just before introducing IP therapy, and than 6 months after start the IP therapy. Method for HbA1c estimation was micro column,

and this method is on the list of standardized methods according National Glycohemoglobin Standardization Program (NSGP) with referent value of HbA1c < 6,0 % for non-diabetic persons (10).

Results

In this paper is analysed metabolic control of T1DM in paediatric patients just before and 6 months after introducing IP therapy. In the period from1st March 2005 to1st September 2008 IP therapy was introduced in 39 paediatric patients with T1DM.

	Age (years)		
	Boys (n=24)	Girls (n=15)	Total (n=39)
Range	5-18	7-16	5-18
x ± SD	12,3±3,5	12,4±2,8	12,3±3,2

TABLE 1. Age range and sex structure of T1DM patients in moment of IP therapy introduction

Age range and sex structure of observed patients are presented on Table 1. Analyzed is metabolic control in 24 boys age range 5-18 years and in 15 girls age range 7-16 years, mean age of all patients was 12,3±3,2 years.

Age groups (years)	Boys	Girls	Total
	N (%)	N (%)	N (%)
1-7	1 (2,6)	1 (2,6)	2 (5,2)
8-14	15(38,5)	9 (23,1)	24 (61,5)
15-18	8 (20,5)	5(12,8)	13 (33,3)
Total	**24 (61,5)**	**15(38,5)**	**39 (100)**

TABLE 2. Sex structure and age groups of T1DM patients in moment of IP therapy introduction

Most T1DM patients (61,5 %) to who we introduced IP therapy were from age group 8-14 years, and less (5,2 %) were younger than 7 years what is presented at Table 2.

T1DM duration	Number of patients	Percent (%)
< 5	17	43,6
5-10	17	43,6
> 10	5	12,8
Total	**39**	**100,0**

TABLE 3. T1DM duration in moment of IP therapy introduction

In the moment of IP therapy introduction same number of patients 17 (43,6 %) had T1DM duration less than five years and from 5 to 10 years what is presented at Table 3.

Therapy	Number of patients	Percent (%)
Classic insulin	15	38,5
Insulin analogues	24	61,5
Total	**39**	**100,0**

TABLE 4. Therapy T1DM patients before IP therapy introduction

Table 4. points out that before IP introduction classic insulin was used by 35,5 % of T1 DM patients and insulin analogues used 61,5 % of T1 DM patients.

HbA1c (%)	Before IP therapy (n)	Before IP therapy (%)	6 months after IP therapy (n)	6 months after IP therapy (%)
<8,0 %	14	35,9	31	79,5
8,0-11,0 %	21	53,9	8	20,5
>11,0 %	4	10,2	0	0
Total	**39**	**100,0**	**39**	**100,0**

TABLE 5. HbA1c values before and 6 months after IP therapy introduction

Most of observed patients 21 (53,9 %) just before IP therapy introduction had HbA1c value in the range between 8 and 11 %. There were less patients (10,2 %) with HbA1c value higher than 11,0 %, and 35,9 % patients had HbA1c values below 8,0 % before IP therapy introduction what is presented at Table 5.

HbA1c (%)	HbA1c before IP therapy (n=39)	HbA1c 6 months after IP therapy (n=39)
Range	6,0 – 14,2	5,9 – 10,0
Mean value (X)	8,57	7,53
Standard deviation (S)	1,65	0,81
Standard error (S x)	0,26	0,12
Median value	8,1	7,4
p	p = 0,0009	

TABLE 6. Correlation in HbA1c values before and 6 months after IP therapy introduction

Table 6. presents mean value of HbA1c before IP therapy introduction was 8,57 % with standard deviation 1,65 %, and 6 months after IP therapy introduction HbA1c value was 7,53 % with standard deviation 0,81 %. Correlation between these values was highly significant p = 0,0009.

Discussion

IP therapy was introduced in 39 T1DM children what is 25 % of total number of T1DM patients up to 18 years old in Canton Sarajevo (11). Percent of patients with IP therapy comparing with the total number of treated T1DM patients in some studies is between 20-50 % (3, 12). There were more boys (61,5 %) with introduced IP therapy what is correspondent with higher incidence of T1DM in boys (13) . IP therapy was introduced mostly in the patients of age range between 8-14 years what is coincident with the period of intensive activity and schooling and is

also coincident with pubertal period of fast growth and development. Swan et al. indicate that the start of fast-acting insulin analogue action is postponed in the period of puberty compared with pre pubertal patients (14). We introduced IP therapy in T1DM patient after remission period what is relative to 1 year T1DM duration. Longer duration of T1DM is correspondent to worse metabolic regulation of the illness (15). In the moment of IP introduction from the total number of observed patients (39) in 22 (56,4 %) of them had T1DM duration longer then 5 years. IP therapy in this patients should be very useful in attaining long-lasting better metabolic control of T1DM (16, 17). Before IP therapy introduction 24 (61,4 %) patients used intensive insulin therapy with insulin analogues. Numerous studies confirmed significantly better metabolic control of T1DM using IP therapy than using classic insulin or insulin analogues like intensive therapy (18, 19). Average level of metabolic control represented by HbA1c level was in our patients in range of unsatisfied values (8,57 %) before introduction of IP therapy. 64,1 % of all patients had HbA1c level higher than 8,0 % before IP therapy. Six months after IP therapy introducing level of HbA1c dropped significantly (p = 0,0009) to mean value of 7,53 %. Even 79,5 % of all patients reached HbA1c level less than 8,0 % after IP therapy started. Sulli and Shashaj reported about significant reduction of HbA1c for 0,7 % in children with T1DM after 1 year long use of IP therapy (20). Nimri et al. reported about reduction of HbA1c level was 0,51 % in the first year of IP therapy of paediatric patients, and reduction was highest in those children who had HbA1c level over 10,0 % before IP therapy (4) . Our study points out that only 20,5 % of all observed patients had HbA1c level over 8,0 % after 6 months long IP therapy, and there were no patient with HbA1c level over 11,0 %. Before start of IP therapy there were 53,9 % of our patients with HbA1c in the range between 8,0-11,0 %, and 10,2 % of patients with HbA1c value over 11,0 %. Spanish authors' study reported about reduction level of HbA1c from 8,12 ± 1,46 % to 7,52 ± 0,87 % even two months after start of IP therapy in children (21). Long- lasting good metabolic control attaining is the aim of complete management of this disease. Every therapy that will help to reduce HbA1c level under 7,0 % is desirable and justified. Our study confirmed IP therapy like mean for attaining better metabolic control of T1DM in children and adolescents. DCCT study pointed out connection between HbA1c level and incidence of appearing and progression of chronic micro vascular complications of diabetes, and its following study: EDIC study confirmed significance of each period of good metabolic control in the life of T1DM patient (22). Periods of good metabolic control of diabetes with HbA1c level les then 7,0 % are "memorized" and protect patient from appearance and progression of micro vascular complications (23). That is why each reduction of HbA1c value towards goal value is extraordinary important in children who must live whole life with their T1DM.

Conclusion

IP therapy introduced in paediatric T1DM patients treated at Paediatric Clinic in Sarajevo proved significantly (p=0,0009) better metabolic regulation of diabetes just after six months' long term treatment. Our results are comparable to other groups referring to effects of IP therapy in paediatric patients.

List of Abbreviations

T1DM	-	TYPE 1 Diabetes mellitus
IP	-	insulin pump
HbA1c	-	glycosylated haemoglobin
NSGP	-	National Glycohemoglobin Standardisation Program (NSGP)
DCCT	-	Diabetes Control and Complication Study
EDIC	-	Epidemiology of Diabetes Interventions and Complications

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