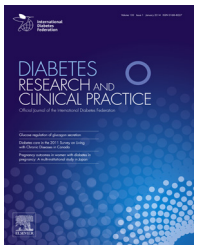
Contents available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

International Diabetes Federation



Impact of insulin pump therapy on long-term glycemic control in a pediatric Spanish cohort

Esmeralda Colino [*], *María Martín-Frías*, *Rosa Yelmo*, *M Ángeles Álvarez*, *Belén Roldán*, *Raquel Barrio* [**]

Pediatric Diabetes Unit, Ramón y Cajal Hospital, Alcalá University, Crta Colmenar km 9,100, 28034 Madrid, Spain

ARTICLE INFO

Article history:
Received 11 November 2015
Received in revised form
8 January 2016
Accepted 8 January 2016
Available online 1 February 2016

Keywords:
Continuous subcutaneous insulin infusion
Pediatric age
Glycemic control
ISPAD/IDF HbA1c recommendations

ABSTRACT

Aims: To evaluate the efficacy and safety of Continuous Subcutaneous Insulin Infusion (CSII) in a pediatric cohort and to determine if the ISPAD/IDF/ADA criteria for good metabolic control are achieved during long periods of time.

Methods: Retrospective longitudinal study including ninety patients [10.5 (6.5–13.9) years of age, 58% males]. Age at debut, type 1 diabetes mellitus duration, pubertal stage, HbA1c, insulin dose, mean number of glycemic controls, number of basal rates, % basal/total insulin, severe hypoglycemia and diabetic ketoacidosis events were analyzed. Subgroup analysis based on age and pubertal stage was performed.

Results: HbA1c decreased from 6.9% [52 mmol/mol] to 6.7% [50 mmol/mol] after one year of CSII. Afterwards, it remained less than 7% during the follow-up period (median 3.5 ± 1.8 years (range 1–8). Prior to CSII, 76% of the subjects met ISPAD/ADA criteria. One year after initiating CSII, 96% of children had HbA1c < 7.5%. Improvement in glycohemoglobin levels was most prominent in those patients with the highest HbA1c initial levels. Total insulin dose decreased from 0.89 to 0.73 UI/kg/day ($p < 0.001$). Proportion of basal/total insulin changed significantly (47 to 42% ($p < 0.05$)). Number of fractions of the basal rate increased from 5.6 ± 1.8 at one year of CSII to 6.7 ± 2.1 five years later. Incidence of severe hypoglycemic events decreased from 19 to 6.9 episodes/100 patient-year. Only 2 episodes of diabetic ketoacidosis occurred.

Conclusions: CSII allows reaching ISPAD/IDF/ADA goals safely during an extended follow-up period in a diabetic pediatric cohort.

1. Introduction

The Diabetes Control and Complications Trial reported that intensive treatment of type 1 diabetes (T1D) led to a reduction in the development and progression of microvascular complications [1]. Furthermore, there are increasing data suggesting that the developing brain in young children with T1D is vulnerable to chronic hyperglycemia, acute hypoglycemia and glucose variability [2,3]. A recent study by Mazaika has shown that type 1 diabetes is associated with significantly reduced growth rate of gray and white matter volume, and have suggested that fluctuations of glucose levels may be associated with the changeability in the brain volume [4]. As a result, current guidelines recommend that treatment of children and adolescents with T1D should aim to achieve near normal

* *Corresponding author*. Tel.: +34 653689857; fax: +34 913368417.
** *Corresponding author*. Tel.: +34 913368646; +fax 34 913368417.
E-mail addresses: esmcol@yahoo.es (E. Colino), raquel.barrio@salud.madrid.org (R. Barrio).
http://dx.doi.org/10.1016/j.diabres.2016.01.012

glycemia without increasing hypoglycemic events. The International Society for Pediatric and Adolescent Diabetes (ISPAD) [5] and the International Diabetes Federation (IDF) recommended a single HbA1c target across all pediatric age-groups. Recently, the American Diabetes Association (ADA) accepted ISPAD and IDF recommendations to maintain HbA1c levels lower than 7.5% during all pediatric age [6]. This, however, seems to be difficult to achieve and maintain in clinical practice [7–10].

Continuous subcutaneous insulin infusion (CSII) offers the most physiological method of insulin supplementation because it allows simulating the normal pattern of daily insulin secretion, superimposed by prandial or correction boluses. Most studies have found that CSII improves HbA1c, although some have reported no improvement or only an initial improvement followed by a return to prepump levels [11–16]. In addition, most of them are limited by the short period of CSII treatment. Recently, some studies have been published with data encompassing longer periods of follow-up [17–19] that have demonstrated an improvement in HbA1c levels, but these are higher than the goals recommended by the International Diabetes Societies for pediatric care.

Our hypotheses are that CSII is effective and safe in pediatric patients, that the initial improvement can last a long period of time, and that CSII allows achieving and maintaining good metabolic control, based on ISPAD/IDF/ADA recommendations.

The primary aims of our study are to evaluate the efficacy and safety of CSII treatment in pediatric patients and to determine if ISPAD/IDF/ADA HbA1c goals are achieved. The secondary objective is to analyze the general and specific characteristics of our pediatric patients depending on age and pubertal stage.

2. Subjects, materials and methods

2.1. Subjects

This is a retrospective longitudinal study of patients with T1D followed at the Pediatric Diabetes Unit at Ramón y Cajal Hospital, a tertiary care center. The subjects were switched to CSII treatment between 2003 and 2012. Data were collected by reviewing charts retrospectively for 1 year before and a minimum of 1 year after CSII treatment started. Exclusion criteria were being >18 years of age, and/or having a concomitant disease that could interfere with the metabolic control of the T1D. Eight patients were excluded (two with severe social problems, two with eating disorders, one with gastroparesia, one with morbid obesity who required bariatric surgery, one with a psychiatric severe disease and one with Munchausen syndrome). Ninety patients were included. Median follow-up period of the total cohort was 3.5 ± 1.8 years (range 1–8).

2.2. Methods

Age, sex, height, weight, HbA1c, insulin doses (UI/kg/day), insulin/carbohydrate ratios, number of basal rates per day, blood glucose monitoring frequency, severe hypoglycemia events, and diabetic ketoacidosis (DKA) episodes were recorded at each clinical visit. Body mass index (BMI) was calculated as weight/height^2 (kg/m^2). Anthropometric data were converted to standard deviation scores by using Spanish scores from Hernandez [20]. HbA1c was measured by using the HPLC method (Menarini, normal value 5.1 ± 0.31%) calibrated to DCCT and IFCC equivalent numbers. The average of three consecutive determinations of HbA1c was considered for the analysis. Severe hypoglycemia was defined as an event with symptoms consistent with hypoglycemia in which the patient required assistance from another person (in pubertad kids) or resulted in seizure/coma [1]. Incidence rate of severe hypoglycemic episodes was calculated as number of episodes per 100 patients-year. Patients were classified in three different groups: preschoolers (≤6 years old), prepubertal (6 years to Tanner stage 2) and pubertal. Patients who had at least Tanner 2 breast development or testicular volume ≥4 ml were included in the pubertal group [21].

2.3. Protocol for pump initiation

Prior to CSII therapy all patients were assessed by the diabetes team for suitability for pump therapy. Insulin pumps and expendables were funded through the Spanish Public Health Care System.

Most patients were changed to CSII therapy in an attempt to improve their glycemic control (decrease HbA1c levels and/or reduce glucose variability), decrease hypoglycemia events and/or improve quality of life.

Before initiating pump therapy, all patients and their families completed the diabetes unit training program. General knowledge of diabetes was evaluated the week before CSII implementation. Our education program on insulin pumps consists of 25 h of instruction (over a period of 4 consecutive days). Prior to CSII initiation, all patients used carbohydrate counting. Throughout the four days of training, frequent blood glucose monitoring was used to determine basal rates, insulin carbohydrates ratios and correction boluses. Insulin correction boluses were recommended if international glycemic objectives were not reached [22]. After beginning CSII treatment, patients and their families had daily telephone contact with the Pediatric Diabetes Unit. First and second clinical visits were at one and four weeks after CSII implementation. Subsequent routine follow-up consisted of one visit every two and a half months. Glucose meters and insulin pump data were downloaded and analyzed at each clinical visit. Glycemic goals were also discussed, and if they were not accomplished, more intensive education was provided. Patients were instructed to change infusion sets at least every 2–3 days. The team was available 24 h a day for calls, WhatsApp, faxes or e-mails.

The study was performed with approval from the Ethics Committee of our Institution.

2.4. Statistical analysis

Statistical analysis of the data was performed using SPSS (Evanston, IL) 21.0 for Windows. Descriptive analysis was done using absolute and relative frequencies for qualitative variables. Mean, median and interquartile range (25–75th) or global range (minimum–maximum) were used for quantitative variables.