

Long-term Follow-up and Efficacy Analysis of Continuous Subcutaneous Insulin Infusion in Children with Type 1 Diabetes Mellitus in Qingdao

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Abstract: To investigate glyceemic control in children with type 1 diabetes mellitus (T1DM) who used of continuous subcutaneous insulin infusion (CSII) in Qingdao area, to explore the CSII in long-term curative effect in treatment of children with T1DM, to analyze the related factors that influence the effect of CSII on T1DM, and to provide guidance for the follow-up management of CSII in long-term therapy. A self-made questionnaire was used to investigate 60 T1DM children who were followed up in the Department of Endocrinology of Qingdao Women and Children Hospital. The purpose was to understand the general situation of children and treatment-related information. The most recent mean Glycosylated Hemoglobin A1c (HbA1c) was (7.12±1.11)% in children with T1DM who were treated with CSII, and the overall control level was good, which was significantly lower than the last mean HbA1c (9.58±2.08)% before CSII treatment. There was a significant difference in the HbA1c level before and after CSII treatment ($P < 0.05$). There were significant differences in the HbA1c level before and after CSII treatment in diet control, daily exercise time, frequency of visit and self-monitoring frequency of blood glucose ($P < 0.05$). After treatment with CSII, the glyceemic control level of T1DM children in Qingdao area was well controlled, and the blood glucose was improved obviously, among which good diet control, regular exercise, regular follow-up visits and especially high-frequency blood glucose monitoring are all conducive to blood glucose control.

Keywords: Type 1 diabetes mellitus in children; Continuous Subcutaneous insulin Infusion; Curative effect; Influence factor; Long-term follow-up

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1. Introduction

Type 1 Diabetes Mellitus (T1DM) is a disorder of glycometabolism in which the production of insulin is reduced because of the destruction of the beta cells in the pancreas caused by autoimmunity. In recent years, the incidence of T1DM in children is increasing all over the world, which has attracted extensive attention in pediatric clinic [1-3]. Continuous subcutaneous insulin infusion (CSII), as an important method for the treatment of intensive therapy of T1DM, has also been widely used internationally [4-6].

There have been extensive and in-depth studies on long-term CSII treatment. However, in China, there is only some areas of CSII treatment of adult T1DM evaluation, but still a lack of studies on long-term follow-up and efficacy evaluation of children with long-term pump. In this study, the long-term follow-up of CSII patients of children in Qingdao was carried out to evaluate the therapeutic effect of CSII and analyze the influencing factors of blood sugar control, so as to better control blood glucose, enhance the treatment satisfaction and improve the quality of life.

2. Subjects and methods

2.1. Subjects

The subjects of this study were 60 children with T1DM. All children with T1DM met the diagnostic criteria of the World Health Organization (WHO) and the American Diabetes Association (ADA) in 1999 [7, 8]. The children lived in Qingdao for a long time, aged 1-18, were treated with Medtronic 722 insulin pump for more than 6 months and followed up in the endocrinology clinic of Qingdao Children and Women's Hospital for a long time.

2.2. Survey content

The self-made questionnaire included the patient's general situation (sex, age, weight, course of disease, duration, family income, main managers of blood sugar and their educational background, occupation, etc.) and the information related to treatment (diet control, time of daily exercise, frequency of seeing a doctor again, frequency of self-monitoring blood sugar, frequency of hypoglycemia, insulin dosage, the control level of glycosylated hemoglobin

A1c(HbA1c), etc.). The blood glucose control standard of the International Society for Pediatric and Adolescent Diabetes (ISPAD) [9]: HbA1c < 7.5% is well controlled, 7.5% ≤ HbA1c ≤ 9.0% is moderately controlled, and HbA1c > 9.0% is poorly controlled.

2.3. Survey method

T1DM children who were followed up in the Department of Endocrinology of Qingdao Women and Children's Hospital were investigated by a questionnaire. The significance and matters needing attention were fully explained to the children and their parents and obtain their permission before the questionnaire was answered. This study was approved by the hospital ethics committee. A total of 60 questionnaires were distributed and 40 valid questionnaires were recovered, with an effective recovery rate of 66.7%.

2.4. Statistical analysis

The collected data were input and analyzed by SPSS 21.0 statistical software. The measurement data is expressed as $\bar{x} \pm s$. T test was used for the normal distribution, the rank sum test was used for the non-normal distribution, and the chi-square test was used for the qualitative data. The difference was statistically significant with $P < 0.05$.

3. Results

3.1. Causes of CSII treatment in T1DM children in Qingdao area

Among the 40 cases, 21 were male and 19 were female. The age ranged from 1.9 to 17.3 years. The average age was 11.2 ± 3.9 years. The course of disease ranged from 0.8 to 11.3 years. The average course ranged from 4.1 ± 2.9 years. The duration ranged from 0.6 to 9.0 years, the average time is 2.7 ± 2.1 years. 67.5% of them were for more stable blood sugar control, 22.5% for fewer injections, and 10% for a more liberal diet. In the processes of pump treatment, 6 children had CSII exclusion for inconvenience, long-term needle implantation and social impact, but they still were chosen to continue treatment.

3.2. Effect of CSII treatment in T1DM children in Qingdao area

The mean HbA1c of the last time before CSII treatment was $(9.58 \pm 2.08)\%$. The rate of reaching the standard was 12.5%, of which HbA1c > 9.0% was as up to 50%. After CSII treatment, the last average

HbA1c was $(7.12 \pm 1.11)\%$. The overall control level was good. The rate of reaching the standard was 62.5%, of which HbA1c > 9.0% only accounted for 2.5%, significantly decreased compared with pre-pump treatment. There was a significant difference in HbA1c level before and after CSII treatment ($P < 0.05$).

3.3. Influencing factors of blood glucose control in T1DM children in Qingdao area

There were significant differences in blood glucose control on age. The control of blood glucose in preschool children was better than that in school age and adolescence. Diet control, daily exercise time, frequency of follow-up visits and self-monitoring of blood glucose were the important factors influencing the therapeutic effect of CSII. There were no significant differences in HbA1c level before and after CSII treatment among gender, glucose manager, manager's education background, manager's occupation and family income (Table 1).

4. Discussion

T1DM in children and adolescents is due to the destruction of insulin-producing islet cells in the body, which makes the body absolutely deficient in its own insulin, and must be treated with insulin for life, also known as insulin-dependent diabetes. At present, it is a chronic disease that seriously affects children's health. Insulin administration can be divided into traditional therapy and intensive therapy. The traditional treatment is by insulin injections of 1-2 times a day. Intensive treatment included multiple daily insulin injections (MDI) or CSII.

With the appearance of fast-acting insulin analog and long-acting insulin analog, as well as the renewal of CSII, CSII has not only become smaller and more beautiful in appearance, but also increasingly perfect in function. Now CSII has become one of the important ways of intensive treatment of T1DM, and CSII intensive therapy has been used more and more widely in clinical practice worldwide [10]. CSII is the most suitable physiological model of insulin therapy, according to a joint statement by several European and American Societies [11]. Multiple studies at home and abroad have shown that CSII can better control blood glucose, effectively reduce HbA1c, and reduce the risk of severe hypoglycemia and diabetic Ketoacidosis [4, 12, 13]. HbA1c is an important index reflecting the level of blood glucose control. Children in the younger age group live irregular lives and have difficulty in controlling their diet. During puberty, on the one hand, sex hormones antagonize insulin, leading to high blood glucose fluctuations.

Table 1. Influencing factors of blood glucose control in T1DM children in Qingdao area

Influencing factor		Number of examples	HbA1c (X±S)	Check value	p-Value
gender	male	21	7.03±0.99	2.211	0.589
	female	19	7.22±1.23		
age (year)	<7year	5	6.06±0.92	0.129	0.020
	≥7year	35	7.27±1.05		
glucose manager	child	5	7.62±1.02	1.100	0.362
	mother	27	7.02±1.15		
	father	5	6.72±0.85		
	elder	3	7.87±1.10		
manager's education	high school and above	25	7.24±0.96	1.895	0.165
	Junior College	10	7.25±1.48		
	Bachelor degree or	5	6.24±0.59		
family income (Ten thousand /year)	<10	34	7.15±1.05	0.191	0.827
	10-20	3	7.13±2.32		
	>20	3	6.73±0.25		
diet control	follow	27	6.84±1.05	0.016	0.019
	don't follow	13	7.70±1.02		
daily exercise time (minute/day)	<30	13	7.88±1.13	5.626	0.007
	30-60	20	6.73±0.10		
	>60	7	6.84±0.61		
frequency of follow-up visits (month/time)	3-6	22	6.77±0.93	4.084	0.025
	6-12	12	7.28±1.25		
	>12	6	8.08±0.86		
self-monitoring of blood glucose (times/day)	≤2	13	7.58±0.81	5.772	0.007
	3-5	11	7.53±1.41		
	≥6	16	6.47±1.01		

On the other hand, they suffer from high levels of psychological stress and heavy negative emotions, making diabetes management more difficult. CSII is expensive, due to the limitations of medicare, not into the medical assistance system, so that CSII study is even less. The goal of diabetes management is to minimize the incidence of hypoglycemia and diabetic Ketoacidosis, and to prevent and delay the occurrence of chronic complications of T1DM.

Since January 1, 2015, CSII was first included in the Qingdao Social Medical Insurance Special Medicine (special material) rescue project, the recipients are people who under the age of 18 years old in Qingdao area and suffering from T1DM urban and rural medical insurance participants. Based on the introduction of insulin pump into the health care system in Qingdao area, the number of children with pump increased significantly, with an increase about 47%-50%. The American Diabetes Association (ADA), in a statement[14], recommends that children and adolescents with T1DM have a glycemic control range of HbA1c < 7.5%. In this study, the mean HbA1c level of T1DM children in Qingdao was $(7.12 \pm 1.1)\%$, and the overall control level was good. Compared with the 68 T1DM children mean HbA1c was $(8.38 \pm 1.55)\%$ investigated by Yujie Han in Qingdao in 2017[15]. The blood glucose control was significantly improved. To analyze the reasons for the good control of HbA1c in this study: Firstly, the selected subjects of study were all children diagnosed in Qingdao Women's and Children's Hospital. The children and their parents were fully educated to make them have a certain understanding of the disease. Small sugar friends and parents communicate with each other when they attend the annual regular organization of diabetes camp activities, which more conducive to blood sugar control. Secondly, questionnaire survey was adopted, the children and their parents who could participate in the study had high compliance. The blood glucose of the children was relatively well controlled, and there was selection bias. Last but not the least, the contents of the questionnaire were filled in by the children and their parents. The results of relevant laboratory tests were not formally reported. So parents would appear recall bias, resulting in some error in the results. Therefore, the method and scheme design of this research would reduce the reliability and accuracy of the conclusion. Due to the small sample size and limited study subjects in Qingdao area. The limited source of cases, the results of this study were one-sided and could not represent the overall situation of CSII treatment in China.

Several studies have shown that self-monitoring of blood glucose at higher frequencies can improve glycemic control. Real-time continuous glucose monitoring (rt-CGM) can continuously monitor the

blood glucose level, showing the whole 24-hour fluctuation of blood glucose, providing the basis for more accurate adjustment of insulin dosage, and optimizing the management of diabetes. In this study, the mean HbA1c was of the 13 children who were monitored with continuous glucose monitoring, compared with the children who were monitored multiple daily glucose monitoring, indicating that higher frequency monitoring led to better glucose control. Haiyan Wei[16] randomly divided 96 children into groups. The study showed that the children treated with "3C" therapy had a definite clinical effect, which could better control blood sugar, shorten the time to reach the standard and reduce the dosage of insulin. At the same time effectively reduced the incidence of hypoglycemia. Although CSII can flexibly adjust the dosage of insulin, if it cannot reflect the changes of blood glucose through the monitoring of blood glucose at a higher frequency. It cannot adjust in time, and it is difficult to better control blood glucose. In order to better control children's blood glucose, it is very important to choose the appropriate frequency of self-monitoring blood glucose.

5. Conclusion

To sum up, the overall level of blood glucose control of children treated with CSII in Qingdao is good, among which diet control, daily exercise time, frequency of follow-up visits and frequency of self-monitoring of blood glucose are all important factors influencing the therapeutic effect of CSII. In order to control blood glucose better, it is necessary to strengthen the frequency of blood glucose monitoring, and cooperate with the use of rt-CGM to better control blood glucose. CSII can carry out insulin regulation timely according to their own situation, so that children with diabetes blood glucose was effectively controlled and the children's quality of life was improved to a greater extent. This study still lacks a systematic evaluation on the satisfaction and quality of life of the children and their families, which needs further study in the future.

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