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Subcutaneous Insulin Infusion Versus Multiple Administrations of Insulin Analogs: Is Either Method Associated with Better Quality of Life in Pediatric Patients with Type 1 Diabetes Mellitus?

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Abstract

Objectives – Type 1 Diabetes Mellitus (DM1) requires demanding treatment in order to achieve good metabolic control. Our aim was to assess whether either method of insulin administration (multiple daily administrations of insulin analogues (MDIA) or continuous subcutaneous insulin infusion (CSII)) is associated with better health-related quality of life (HRQoL). **Methods** – We conducted a cross-sectional study. Patients aged 10-18 years with a disease duration of at least six months were included. HRQoL was assessed by having patients and their caregivers complete the DISABKIDS-37 questionnaire. **Results** – Of the 40 patients included, 22 (55%) had CSII. There were no statistically significant differences between subscale scores and overall HRQoL between patients or between parents of patients with CSII or MDIA. CSII patients and parents scored better on all subscales and on the total scale, although without statistically significant differences. There were no statistically significant differences in the subscale scores and overall HRQoL reported by the patients and their parents, but there was a strong correlation between the children's and parents' scores (R=0.770; P<0.01), which was similar in patients with CSII or MDIA (R=0.735 vs R=0.790). **Conclusion** – Although we did not identify statistically significant differences, there was a trend towards a better HRQoL associated with the use of CSII, both from the perspective of the adolescents and their parents. This could influence therapeutic choice. Consistency between the assessments of adolescents and their carers was observed. The choice between MDIA and CSII should be based on individual preferences in order to optimize the HRQoL of adolescents with DM1.

Key Words: Type 1 Diabetes Mellitus ▪ HRQoL ▪ Insulin Administration ▪ Metabolic Control.

Introduction

Type 1 diabetes (T1D) is one the most common chronic diseases in childhood with a prevalence and incidence that varies around the world (1-4). In 2021, there were an estimated 108,300 children and adolescents under the age of 15 newly diagnosed with type 1 diabetes, and 651,700 children and adolescents living with the condition worldwide (5). T1D is characterized by the destruction of the ß-cells, usually by an autoimmune process, resulting in loss of endogenous insulin production (5).

In order to diminish long term sequelae of the disease, such as retinopathy, nephropathy and neuropathy, tight glycemic control is required, being best achieved through intensive regimens on insulin treatment (7). Currently there are two available options to achieve this: multiple daily administrations of insulin analogues (MDIA) or Continuous subcutaneous insulin infusion (CSII). However,

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it's worth noting that nowadays, with the advent of technology in diabetes as well, different CSII systems are available that are increasingly sophisticated (8).

T1DM treatment is continuous and very demanding, including multiple daily subcutaneous insulin administrations, blood glucose monitoring, dietary planning, physical activity, and frequent medical consultations, with an impact on health-related quality of life (HRQoL) (9).

Despite MDIAA still being the first-line therapy in many regions around the world, CSII is gaining popularity among pediatric patients and is considered a valid option in multiple guidelines (8, 10-12). Currently, the literature is still inconsistent on the superiority of either method in reaching therapeutic targets, with some articles demonstrating the benefit of CSII and others showing no difference between the two methods (13-17). Although it is well recognized that the treatment of T1D impairs HRQoL, the literature is inconsistent on the superiority of any of the methods, and there are few studies comparing them (17-20).

The aim of this study was to compare HRQoL in patients with different diabetes management methods.

Methods

A cross-sectional study was carried out between January and September 2023. The questionnaire DISABKIDS-37 in the Portuguese version was applied to adolescents, and their caregivers, managed at Pediatric Diabetes consultation of a level II hospital, aged between 10 and 18 years. Only patients with at least 6 months of T1DM were included, and patients with health conditions that prevented them from understanding the questionnaire were excluded. The primary objective was to assess HRQoL in both groups, CSII and MDIA, as perceived by patients and caregivers and compare both groups. In Portugal, T1DM therapy is free, so we believe that the economic burden of the disease did not influence the assessment of quality of life.

Data was collected between February and August 2023, at one single time for each patient. Besides the questionnaire, some demographic data (e.g. age, gender, age of diagnosis, date of diagnosis) and clinical indicators for T1DM control, as HbA1c level, were collected accessing the medical file with the caregiver's authorization. A value of HbA1c below 7% was considered good metabolic control.

DISABKIDS-37 module is designed to assess HRQoL in children and adolescents, aged between 8 and 18 years, with any chronic condition. There are two versions, one for the children/adolescent and one for the caregivers. The questionnaire includes 37 items, which are similar in both self and proxy versions, relating to the child's global functioning and well-being during the last four weeks. A five-point Likert response scale is adopted in both versions of the instrument (1=Never; 2=Seldom; 3=Quite often; 4=Very often; 5=Always), although negative items (8–25 and 32–37) need to be recoded inversely. The 37 questions are grouped into six facets: independence; emotion; social inclusion; social exclusion; physical limitation; and treatment. The global raw score (minimum=37, maximum=215) represents the computation of these six facets, thus considering HRQoL as a second-order construct (19). The validated Portuguese version was used. Raw DISABKIDS 37 score was transformed into a 0-100 scale.

Ethics Statement

Caregivers provided their informed consent to participate in the study and to release information. The study was approved by the hospitals' Ethics Committee in accordance with local and national regulations (Nº 69/2023).

Statistical Analyses

Data are reported as mean±SD or median (IQR), according to the normality of the variable, normal or not normal, respectively. Statistical analysis was performed using IBM SPSS Advanced Statistics 26.0 (5725-A54). Comparisons of baseline data between the two groups were performed

using two-sided Student's *t* test. The chi-square test was used for comparing dichotomous variables. The Mann-Whitney U test was used to compare the scores between the two groups, Wilcoxon test to compare medians between paired variables and Spearman's correlation coefficient was used to assess the association between continuous variables. A P value smaller than 0.05 was considered statistically significant.

Results

A total of 52 patients fit the inclusion criteria, 28 with CSII and 24 with MDIAA. Of those, 40 accepted to participate in the study, as well as the same number of caregivers (one for each adolescent). The first group, MDIA group, was composed of 18 patients, 10 (55,6%) were female and the mean age was 15.22 years (SD=2.32). The mean HbA1c was 9.01% (SD=2.55). The mean time since diagnosis was 4.83 years (SD=3,51). The second group, CSII group, consisted of 22 patients. Of those, 14 (63,6%) were male and the mean age was 14,23 years (SD=2,16). The mean HbA1c was 7,65% (SD=1,01). The mean time since diagnosis was 7,39 years (SD=2,44). No significative differences were found between the two groups concerning age (P=0.709) or gender distribution (P=0.225). HbA1c was significantly higher in the MDIA group (P=0,046) and the time since diagnosis was significantly higher in the CSII group (P=0,014).

HRQoL Perceived by Patients

The median for HRQoL was 78.2 (65.03; 88.68) in the MDIA group and 73.31 (58.45; 82.93) in the CSII group. There were no significant differences between the groups (P=0.229). Analyzing the six facets of the questionnaires, there were no significant differences in any of the categories. However, the CSII scored higher in the total scale and in all subscales.

In the MDIA group we found a significant negative correlation between HbA1c and perceived HRQoL (R=-0.534; P=0.022). The same was not verified in the CSII group. Although the correlation was negative, it wasn't significant (R=-0.312; P=0.157). There were no significant correlations with length of illness or age in any of the groups.

HRQoL Perceived by Caregivers

This questionnaire is designed to evaluate the caregivers' perception of their adolescents' HRQoL. The median for HRQoL was 71,62 (54.73;81.25) in the caregivers of the MDIA group and 71,96 (61.82; 86.82) in the CSII group. There were no significant differences between the groups of caregivers (P=0.446). Analyzing the six facets of the questionnaires, there were no significant differences in any of the categories. As in the patients' group, the CSII group scored higher in the total scale and in all subscales, with the exception of the social exclusion subscale, where the group of MDIA scored higher

Table 1. HRQoL Perceived by Patients (Score (IQR))

Scale	CSII Group	MDIA Group	U	P
Independence subscale	85.4 (70.8;91.7)	83.3 (P25-61.5; P75-88.5)	167.5	0.411
Physical limitation subscale	81.2 (54.2; 87.5)	70.8 (P25-61.4; P75-80.2)	163.0	0.339
Emotions subscale	73.2 (45.5; 89.3)	58.9 (47.3; 70.5)	144.5	0.145
Social exclusion subscale	91.7 (75.0; 95.8)	81.2 (70.8; 91.6)	150.5	0.193
Social inclusion subscale	83.3 (78.1; 91.7)	83.3 (76.0; 91.7)	184.5	0.711
Treatment subscale	75.0 (50.0;89.6)	75.0 (41.7; 83.3)	163.5	0.659
Global HRQoL	78.2 (65.0;88.7)	73.3 (58.5; 82.9)	153.0	0.221

CSII=Continuous subcutaneous insulin infusion; HRQoL=Health related quality of life; MDIA=Multiple daily administrations of insulin analogues; U=Mann–Whitney U test.

Table 2. HRQoL Perceived by Caregivers (Score (IQR))

Scale	CSII Group	MDIA Group	U	P
Independence subscale	83.3 (66.7; 91.7)	77.1 (57.3; 88.5)	168.5	0.420
Physical limitation subscale	68.8 (49.0; P75-88.5)	66.7 (59.4; 75.0)	187.0	0.764
Emotions subscale	67.9 (49.1; 83.0)	55.4 (50.0; 64.3)	148.0	0.173
Social exclusion subscale	75.0 (61.5; 92.7)	87.5 (68.8; 92.7)	170.0	0.444
Social inclusion subscale	83,3 (69.8; 91.7)	81.3 (68.8; 87.5)	175.5	0.538
Treatment subscale	68.8 (41.7; 87.5)	56.3 (28.1; 76.0)	148.0	0.173
Global HRQoL	72.0 (61.8; 86.8)	71.6 (54.7; 81.3)	170.0	0.446

CSII=Continuous subcutaneous insulin infusion; HRQoL=Health related quality of life; MDIA=Multiple daily administrations of insulin analogues; U=Mann–Whitney U test.

Table 3. Comparison between Patients' and Caregivers' Answers

Patients vs. Caregivers	CSII Group	MDIA Group
Independence subscale	Z=-0.917; P=0.359	Z=-0.569; P=0.569
Physical limitation subscale	Z=-1.687; P=0.92	Z=-0.760; P=0.448
Emotions subscale	Z=-0.504; P=0.614	Z=-0.595; P=0.552
Social exclusion subscale	Z=-1.917; P=0.055	Z=-0.467; P=0.640
Social inclusion subscale	Z=-1.313; P=0.189	Z=-1.164; P=0.244
Treatment subscale	Z=-1.103; P=0.270	Z=0.979; P=0.327
Global HRQoL	Z=-1.185; P=0.236	Z=-1.547; P=0.122

CSII=Continuous subcutaneous insulin infusion; HRQoL=Health related quality of life; MDIA=Multiple daily administrations of insulin analogues; Z =Z-test.

As found in the patients' group, we also found a significant negative correlation between HbA1c and perceived HRQoL (R=-0.550; P=0.018) in the MDIA group. Once again, similarly to the patients, ths was not observed in the CSII group. Although the correlation was negative, It was not significant (R=-0.038; P=0.867). We also found no significant correlations with length of illness or age in any of the groups.

Table 4. Correlation between Patients' and Caregivers' Answers

Groups	R	P*
Patients vs. Caregivers	0.770	<0.01
Patients vs. Caregivers CSII Group	0.735	<0.01
Patients vs. Caregivers MDI Group	0.817	<0.01

CSII=Continuous subcutaneous insulin infusion; MDIA=Multiple daily administrations of insulin analogues; R=Correlation; *Spearman's correlation.

Comparing HRQoL Perceived by Patients versus Caregivers

Comparing the responses to each subscale and the total HRQoL coefficient of the patients and their caregivers, no significant difference was found between the medians on any scale, either in the CSII group or the MDIA group.

Considering both groups, there was a strong correlation between the patients' and the caregivers' answers (R=0.770; P<0,01). Considering the groups individually, we also found also found strong correlation, with a R=0.735 in the CSII group (P<0.01) and a R=0.817 in the MDIA group (P<0.01).

Discussion

In our study we found that, although no statistically significant differences were identified, there was a trend towards better HRQoL associated with the use of CSII, both from the perspective of adolescents and their parents. In the patients' group this information was true for all the subscales. This information could be important for influencing therapeutic choice. In the parents' group it was true for all the subscales, except for the social exclusion subscale where parents of adolescents with MDIA scored higher. We should also highlight that, although there were no significant differences, the parents scored lower in the global HRQoL. However, we found a strong correlation between the evaluations of adolescents and their parents in the global HRQoL and no significant differences when we compare all the subscales, meaning that, although parents perceive HRQoL more negatively than their own children, there is a strong and important consistency in both perceptions. Parents probably experience their children's' day-to-day limitations in relation to diabetes with greater anxiety, perceiving it more negatively than the patient does.

As already mentioned, currently, there is no consensus in the literature as to whether the use of CSII results in a significant improvement in HRQoL in adolescents with DM1, with some studies favoring the last one (17-20). Although some studies report that the use of CSII offers greater flexibility in the day-to-day life of these families, as well as metabolic benefits (18, 22, 23), the truth is that using the pump and carrying it, in terms of aesthetics and mobility, can be a burden for the patient, especially in adolescence, and may be one of the reasons that negatively influences quality of life. In addition, the presence of the pump makes diabetic patients more easily identifiable to third parties, which is one of the reasons why we think that the parents of adolescents with MDIA scored higher on the social exclusion scale.

We also found that there was a strong negative correlation between HRQoL and metabolic control in the MDIA group, warning that the way they deal with the disease will have a greater impact on their disease-related quality of life than the therapeutic approach chosen. The correlation between poorer metabolic control and poorer HRQoL perception has also been described in other studies carried out in the USA and Spain (24, 25). The duration of the disease and the patients' age didn't seem to significantly impact the HRQoL perception in our group.

As a secondary finding of the study, we found a correlation between better HbA1c values in the group with CSII. This finding is consistent with some existing studies (13-17, 20) and may also have an impact on the choice of therapy. However, we have to consider that it is likely that patients selected for CSII have a better prior performance in the therapeutic approach to the disease, so a bias may be present here.

Limitations of the Study

We can highlight some limitations to our study. The first one is the small sample. Extending the sample to, for example, a multicentre study would help alleviate this. Secondly, the allocation of therapeutic approaches was not carried out randomly, and the reasons for using a particular method may in themselves influence HRQoL, such as better metabolic control, greater rigor in the administration of therapy and approach to the disease, and preference for the method itself. In addition, the type of infusion pump was not taken into account in the CSII group, and this could also influence patients' perceptions. Finally, the responses were only made at a single moment and we can not be sure whether the parents' and patients' responses were completely individual.

Conclusion

To the best of our knowledge, this is the first study in Portugal to compare HRQoL in DM1 patients treated with CSII or MDIA. In our study, although we did not observe a significant superiority of CSII, we did observe a trend towards better HRQoL in these patients. We consider that the choice between

MDIA and CSII should be based on individual preferences in order to optimize the HRQoL and metabolic control of adolescents with DM1. However, the better metabolic control in the CSII group should be emphasised, and this fact should also play a role in the decision. More studies and an increased sample size are needed to better understand this trend and explore adolescent preferences in greater detail.

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Conflict of Interest: The authors declare that they have no conflict of interest.

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