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# Glycemic control and weight outcomes after initiation of continuous subcutaneous insulin infusion therapy☆

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ABSTRACT

*Introduction:* The continuous subcutaneous insulin infusion (CSII) is an alternative to multiple daily injections therapy in type 1 diabetes and its use is increasingly common due to the beneficial effects on glucose control.
*Aims:* To analyze clinical features and biochemical parameters of patients on CSII therapy.
*Type of study:* Longitudinal retrospective.
*Setting:* Outpatient clinic.
Population: Type 1 diabetic patients using insulin infusion pump in our department.
*Methods:* We evaluated outcomes regarding the following set points: immediately before initiation of CSII therapy, 12 months after inclusion and in the last appointmentHH. For statistical analysis, we used non-parametric tests and linear regression analysis. We considered significant a value of $p \leq 0.05$.
*Results:* We studied 63 patients (24 men; 39 women) with a mean pre-CSII HbA1c of 8.2% ± 1.43; mean age at the time of placement of 32.7 ± 10.94 years; and mean follow up time after placement of 2.1 ± 1.92 years. There was a statistically significant reduction of HbA1c during follow-up (HbA1c 12 months: 7.2% [6.6–7.8] p = 0.001; HbA1c at the end of follow-up: 7.4% [6.6–7.9] p = 0,001). There was no significant variation of weight or total daily insulin dose. We registered a negative correlation between the last HbA1c before CSII and the reduction in HbA1c until the end of the follow-up period (ρ=−0.644 p = 0.000). The median reduction in HbA1c was higher in women (W: −1.10 [−2.20–−0.40] vs M: −0.10 [−0.80–0.40]; p = 0.002). Female gender was a predictive factor of better results with CSII, even after adjustment to the last HbA1c before the initiation of therapy.
*Conclusions:* In our sample, the last HbA1c before the beginning of CSII was the most powerful predictive factor of the reduction of HbA1c during follow up. Women had better results than men. There was no significant variation of weight and total daily insulin dose during follow up.



## Evolução do controle metabólico e do peso após início de terapêutica de infusão subcutânea contínua de insulina

*Palavras chave:*
Bomba de infusão subcutânea de insulina
*Diabetes mellitus* tipo 1
Gênero

RESUMO

*Introdução:* A terapêutica com infusão subcutânea contínua de insulina (Tisi) é uma opção ao uso de múltiplas injeções de insulina na diabete tipo 1 e o seu uso é cada vez mais frequente dados os benefícios no controle glicêmico.
*Objetivos:* Analisar as características clínicas e os parâmetros bioquímicos dos doentes tratados com Tisi e procurar fatores preditores da resposta à terapêutica.
*Tipo de estudo:* Longitudinal retrospectivo.
*Local:* Consulta externa.
*População:* Diabéticos tipo 1 usuários de Tisi seguidos no nosso serviço.

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*Métodos:* Foram registrados os resultados nos seguintes períodos: imediatamente antes da colocação da Tisi, 12 meses após colocação e à data da última consulta. Os resultados foram apresentados como média ± desvio padrão ou mediana [quartis]. Foram usados testes não paramétricos para a análise estatística e foi efetuada regressão linear. Foram considerados significativos os valores de p < 0,05.
*Resultados:* A amostra era constituída por 63 diabéticos tipo 1 (24 homens - H; 39 mulheres - M) com os seguintes valores antes da colocação: idade 32,7 ± 10,94 anos; HbA1c 8,2% ± 1,43. O tempo médio de catamnese foi de 2,1 ± 1,92 anos. Ocorreu uma redução estatisticamente significativa da HbA1c ao longo do tempo de seguimento (HbA1c aos 12 meses: 7,2% [6,6-8] p = 0,001; HbA1c ao fim do tempo de seguimento: 7,4% [6,6,7,9] p = 0,001). Não se verificou variação do peso e da dose diária total de insulina. Verificou-se uma correlação negativa entre a HbA1c prévia e a redução da HbA1c até ao fim do tempo de seguimento (ρ= −0,644 p = 0,000). A mediana da redução da HbA1c até a data da última consulta foi maior no grupo das mulheres (M: −1,10 [−2,20 - −0,40] *vs*. H: −0,10 [−0,80 - −0,40]; p = 0,002). O gênero feminino foi um fator preditivo de melhor resposta à Tisi mesmo após ajuste para a HbA1c prévia.
*Conclusões:* : Na amostra estudada, a última HbA1c anterior ao início da Tisi foi o fator com maior capacidade de predição da resposta à terapêutica. As mulheres obtiveram melhores resultados da terapêutica com Tisi do que os homens. Não ocorreram variações estatisticamente significativas do peso ou da dose diária total de insulina.



## Introduction

After the publication of the DCCT[1], the goal of the treatment of type 1 diabetes mellitus is to obtain glucose values as near as possible to normal, as long as the patient's hypoglycaemia risk isn't unacceptably high. The optimum glucose control would prevent the occurrence of chronic complications of diabetes[2] and result in improvement of the quality of life of the person with diabetes[3]. The review of target glucose values in type 1 diabetes mellitus has led to the increased use of intensive insulin therapy that was suggested by the same study as the most effective method to obtain the proposed goals.

Continuous subcutaneous insulin infusion (CSII) therapy is an alternative to the use of multiple daily injections (MDI) for the treatment of type 1 diabetes mellitus and its use is increasingly common due to the beneficial effects on glucose control. Pickup[4] used CSII as a research tool to elucidate the relation between glucose control and diabetic complications. Later on, other authors described the improvement of glucose control in selected and motivated patients that previously had not attained the treatment goals with MDI. [5–11]. Although several studies showed significant reductions in HbA1c with CSII, a metanalysis of randomized clinical trials comparing with MDI showed, by a random effects model, a non-significant trend towards mean reductions in HbA1c of −0.26 (IC 95% −0.57-0.05) after 6 months follow up and −0.61 (IC 95% −1.29–0.07) after 12 months follow up[7]. Other authors[12] detected significant reductions in HbA1c (9.36 ± 0.22 vs 8.96 ± 0.11, p = 0.039). Significant differences between therapeutic modalities are only apparent with follow up periods longer than 1 year.

Regarding hypoglycaemia risk, several observational studies suggest that CSII is associated with a significant risk reduction, particularly in terms of severe episodes[7]. The same metanalysis did not find data supporting sustained reductions in total daily insulin dose (TDID) in patients using CSII, nor significant reductions in weight. Other authors[12,13] suggest that CSII might be associated with as much as 16% reductions in TDID comparing with multiple daily injections, as well as a significant increase in weight (68.2 ± 0.7 Kg vs 71.2 ± 0.3 Kg; p < 0.001).

Greater patient satisfaction has been documented in patients using CSII therapy, although there is discordance between studies in terms of impact on quality of life[3,6,7,14]. However, it is of note that CSII therapy might be associated with other complications, namely an increase in risk of diabetic ketoacidosis, pump malfunction and infusion site infections[12]. Few studies have analyzed the variables associated with improved metabolic control after initiation of CSII therapy. Two studies have shown greater benefit in individuals with higher HbA1c before CSII[15,16]. The selection of patients with higher HbA1c (HbA1c > 8.0%) was associated with superior benefit than described in two metanalysis[12,13].

There is no significant data regarding the effect of age in CSII but several authors have suggested good results in pediatric patients in terms of HbA1c reduction as well as in risk of hypoglycaemia and quality of life[17]. One study on female adolescents showed a good response to CSII therapy in this population, which included individuals with eating disorders[18].

## Aims

To analyze the clinical characteristics and biochemical parameters in diabetic patients treated with CSII therapy and identify the predictive factors for a good response to this regimen.

## Methods

We included all individuals with type 1 diabetes that were users of CSII, under follow up in the Endocrinology consultation of our hospital. We recorded variables in the following time points: immediately before initiation of CSII therapy, 12 months after initiating use of the insulin pump and at the time of the last appointment. As the TDID is not recorded in the patient's clinical file, it was inferred from the insulin sensitivity factor, which is calculated using the 1800 rule, universally used in our consultation. Results were presented as mean ± standard deviation or median [quartiles]. Changes in weight, TDID and TDID/Weight ratio were calculated as fractions. For the statistical analysis, we used SPSS Statistics 20.0. To compare differences in the variables and their correlations we used the Wilcoxon test, Mann-Whitney test, Spearman correlation and a linear regression model. We considered significant a value of $p \leq 0.05$. In a separate analysis, the sample was divided in two groups (better and worse response) according to the median of variation in HbA1c at the end of follow up (−0.8%), and we used the Mann-Whitney and Fischer exact tests to compare groups.

## Results

The sample included 63 patients with type 1 diabetes (24 men; 39 women) whose clinical characteristics are presented in Table 1. The mean follow up was 2.08 ± 1.920 years.