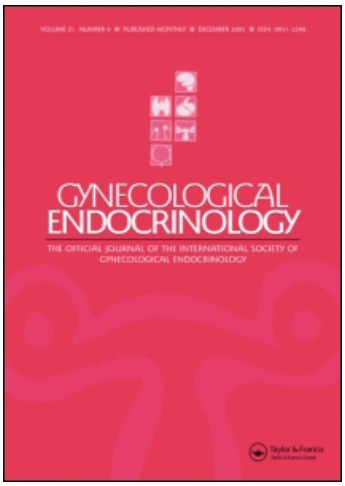

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ORIGINAL PAPER

Continuous subcutaneous insulin infusion and multiple dose insulin injections in Type 1 diabetic pregnant women: a case–control study

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Abstract

The aim of this study was to evaluate the effects of continuous subcutaneous insulin infusion (CSII) on glycemic control and pregnancy outcomes in Type 1 diabetic pregnant women. We retrospectively evaluated 42 subjects, 20 treated with CSII and 22 with multiple dose insulin injections (MDI). The two groups were comparable for age, pre-pregnancy BMI, and primiparous rate, whereas women in the CSII group showed a tendency toward a longer diabetes duration ($p = 0.06$). Pre-pregnancy diabetic retinopathy and/or nephropathy were present in nine women of CSII and three of MDI. In all women metabolic control improved during pregnancy, without differences between the two groups and at the end of gestation HbA1c was 6.3 ± 0.6 in CSII and $6.1 \pm 1.1\%$ in MDI. Moreover, there were no differences in weight gain, whereas insulin requirement resulted significantly ($p = 0.009$) lower in CSII than in MDI. We recorded only one severe hypoglycaemic episode in both groups. No cases of deteriorations of the chronic diabetic complications were observed. The delivery occurred at 36.4 ± 2.2 weeks; birth weight, the rate of large for gestational age, and the parameters of foetal morbidity were similar in both groups. In conclusions, CSII and MDI are both effective in improving maternal glucose control and have both similar pregnancy outcomes.

Keywords: *Insulin pumps, pregnancy, Type 1 diabetes, maternal-foetal outcome*

Introduction

In Type 1 diabetic pregnant women a normoglycaemia before and during pregnancy is essential to reduce the maternal-foetal morbidity and an effective and safe insulin therapy is needed to reach tight glycaemic control [1]. Conventionally, insulin can be provided by multiple daily injections (MDI) or by continuous subcutaneous infusion (CSII). However, CSII has gained in popularity and experience with the treatment of Type 1 diabetic patients has increased [2,3]. Comparable trials with the use of CSII during pregnancy are limited to earlier pump technology [4–7], that did not show significant advantages, but lately greater experience with the use of CSII in pregnancy has yielded a positive attitude toward the use of insulin pumps during pregnancy. Nevertheless, studies comparing the effectiveness of these two modalities during pregnancy are limited and still not conclusive [8,9]. Therefore, we performed this study to compare the effects of CSII over MDI on maternal metabolic control and pregnancy outcomes.

Patients and methods

This retrospective case–control study included 42 Caucasian pregnant women with Type 1 diabetes, treated with CSII ($n = 20$) or MDI ($n = 22$) and monitored at our Outpatient Clinic from January 2005 until June 2008. Women with pumps started this treatment almost 6 months before pregnancy because they failed to achieve satisfactory glycaemic control. They received a therapeutic education programme, specifically addressed to subjects preparing for CSII treatment. Conventional therapy using MDI consisted in three subcutaneous daily

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doses of short insulin analogues before meals and NPH insulin two or three times a day. All the patients received dietary counselling by a dietician and performed self-monitoring of blood glucose (SMBG) almost 6–8 times a day (before and 1 h after meals, at bedtime, and during the night) in order to modify the insulin dose, if necessary. The treatment was aimed to obtain the glucose goals, defined as blood glucose less than 90 mg/dl before meals and 1-h postprandial less than 130 mg/dl.

At baseline, as maternal characteristics we registered age, parity, pre-pregnancy BMI, diabetic complications (retinopathy and nephropathy), insulin dose, and HbA1c. Glucose control was determined each trimester by the HbA1c, the number of severe hypoglycaemia and episodes of ketoacidosis. Maternal hypoglycaemia was considered a hypoglycaemic emergency which requires another person's help, and Ketoacidosis was considered an episode of severe hyperglycaemia with ketosis and dehydration requiring professional intervention. Newborns with a birth-weight >90th percentile on the basis of the standard table for the Italian population [10] were considered large for gestational age (LGA). Foetal morbidity was classified according to the Obstetrical Quality Indicator [11].

Statistical analysis methods

Data were expressed as a mean value and a standard deviation. Statistical analysis was performed using Student's *t* test for paired or unpaired data and the χ^2 test or Fisher exact test. All analysis were performed using a statistical package (Statview SE) on a Macintosh computer.

Results

CSII and MDI groups were comparable for age, pre-pregnancy BMI, and primiparous rate, whereas women in the CSII group showed a tendency toward a longer diabetes duration (CSII: 16.8 ± 8.2 *vs.* MDI: 12.1 ± 7.7 years, $p = 0.06$). Pre-pregnancy diabetic retinopathy and/or nephropathy were present in nine (45%) of CSII and three (13.6%) of MDI women ($p = 0.057$) (Table I).

At the first evaluation during pregnancy (6 ± 2.2 weeks) HbA1c values and daily insulin doses were similar in the two groups (Table II). In all women metabolic control improved during pregnancy, without differences between the two groups. At the end of the pregnancy there were no differences in weight gain and HbA1c values, whereas insulin requirement resulted significantly lower in CSII than in MDI (Table II). We recorded only one severe hypoglycaemic episode in both groups. No episodes of ketoacidosis were observed. Moreover, no cases of deteriorations of the chronic diabetic complications were observed in the two groups.

The delivery occurred at 36.4 ± 2.2 weeks without differences as regards the rate of preterm deliveries and C-sections. All babies were alive at birth without congenital malformations. Birth weight, LGA, SGA, and Apgar Score were comparable. No differences concerning foetal morbidity were observed (Table III).

Table I. Maternal clinical characteristics.

	CSII ($n=20$)	MDI ($n=22$)
Maternal age (years)	31.0 ± 3.0	29.8 ± 6.3
Diabetes duration (years)	16 ± 8.2	12.1 ± 7.7
Nulliparity rate (%)	85	36
Pre-pregnancy BMI (kg/m^2)	23 ± 2.8	23.7 ± 4.3
Women with diabetic retinopathy (*n*)	7	3
Women with diabetic nephropathy (n)	2	0

CSII, continous subcutaneous insulin infusion; MDI, multiple daily injections.

Table II. Maternal outcome.

	CSII ($n=20$)	MDI ($n=22$)
Weight gain (kg)	13.4 ± 5.4	11.5 ± 3.7
HbA1c at 1st evaluation during pregnancy (%)	6.9 ± 0.7	7.4 ± 1.3
HbA1c at the end of pregnancy (%)	6.3 ± 0.6	6.1 ± 1.1
Insulin dose at 1st evaluation during pregnancy (IU/kg)	0.62 ± 0.1	0.69 ± 0.2
Insulin dose at the end of pregnancy (IU/kg)	0.76 ± 0.3	1.1 ± 0.3*
Severe hypoglycaemic episodes (*n*)	1	1
Diabetic ketosis episodes (*n*)	0	0

CSII, continous subcutaneous insulin infusion; MDI, multiple daily injections.
*$p = 0.009$.

Table III. Pregnancy and neonatal outcome.

	CSII ($n=20$)	MDI ($n=22$)
Gestational age at delivery (years)	36.38 ± 2.2	36.35 ± 2.3
Preterm delivery (%)	33	40
Caesarean section (%)	95	94
Birth weight (g)	3295.58 ± 747	3101.84 ± 699
LGA (%)	45	22.7
SGA (%)	5	4.5
Transient hypoglicaemia (*n*)	2	3
Hyperbilirubinemia (*n*)	5	4
NICU admission (*n*)	1	2

CSII, continuos subcutaneous insulin infusion; MDI, multiple daily injections; NICU, neonatal intensive cure unit.

Discussion

This study shows that MDI and CSII are both effective in improving maternal glucose control and both these treatment modalities have similar pregnancy outcomes.

Our results confirm what was found in other studies performed during [12–18] and outside of pregnancy [19], which did not show any metabolic differences of CSII over MDI.

On the other hand our results may mask the possible benefits of CSII. In fact, women of the CSII group were transferred from MDI to CSII because conventional treatment did not allow them to reach an optimal glucose control; in addition they had a longer diabetes duration and a higher rate of diabetic complications than MDI women. Therefore, we can postulate that for these women, with a more instable and severe diabetes, CSII therapy offered an opportunity to have a pregnancy outcome similar to other diabetic women.

As concerns possible disadvantages related to the use of CSII in pregnancy, Chen et al. [20] found higher rates of both maternal ketoacidosis and neonatal hypoglycaemia. Differently, in our study, there were no cases of maternal ketoacidosis and no differences in neonatal hypoglicaemic episodes were observed between the two groups. This could be explained by the fact that our patients received a therapeutic education programme, and that all women were able to control the mechanism of CSII and to modify the insulin delivery correctly.

In our study the nonoptimal glucose control during pregnancy may explain the high rate of LGA and C-sections in both groups. These rates remain elevated despite the achievement of HbA1c value close to 6%. Probably, it is not a sufficient condition to assure an optimal pregnancy outcome, considering that the normal values of HbA1c for pregnant nondiabetic women are between 4.0% and 5.5% (lower than nonpregnant women) [21]. Moreover the number of 6–8 SMBG daily that we prescribed for our patients is not sufficient to control glucose values during pregnancy, because of the rapid changes in glucose concentrations. As reported by Kerssen et al. [22] a minimum of 10 SMBG determinations daily is necessary to obtain adequate information about daily hyperglycaemic excursions during the second and third trimester, which is an important factor for the development of LGA. Therefore, our findings support the need to reach tighter glycaemic control and to prescribe a greater number SMBG determinations in order to minimize the foetal maternal morbidity in diabetic pregnancy, independently of therapy modalities.

In conclusion, our results show similar pregnancy outcomes and maternal glucose control in both MDI and CSII treatment modalities in agreement with what was reported by two recent meta-analysis [8,9]. Therefore, to establish a clear benefit of CSII, large prospective randomized studies are needed to improve therapeutic interventions aimed at achieving normoglycaemia during pregnancy.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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