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Acute Complications and Pregnancy Outcomes with Continuous Subcutaneous Insulin Infusion Therapy in Pregnant Women with Type 1 Diabetes Mellitus

Tip 1 Diabetes Mellitusu Olan Gebelerde Sürekli Subkütan İnsülin İnfüzyon Tedavisinin Akut Komplikasyonlar ve Gebelik Sonlanımı Üzerine Etkisi

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Abstract

Objective: Pregnant women with type 1 diabetes mellitus (T1DM) have increased risk of fetal, maternal, and perinatal complications. In this report, we aimed to evaluate the effects of continuous subcutaneous insulin infusion (CSII) therapy on pregnancy outcomes, glycemic control, and acute complications in pregnant women with T1DM. **Material and Methods:** We retrospectively analyzed the data of 15 women with T1DM who were on CSII therapy during their pregnancy, and who were followed up at our clinic between 2008 and 2014. Acute complications, fetal/maternal, and perinatal complications, and glycemic control were analyzed. **Results:** The mean age of the patients was 28.2±3.6 years, and the mean duration of diabetes was 8±5.4 years. We did not observe severe hypoglycemic episodes and diabetic ketoacidosis during their pregnancy. The mean HbA1c levels at 4-8 weeks of pregnancy decreased from 7.4±1.3% to 6.3±0.7% at 34-38 weeks of pregnancy. The mean duration of pregnancy and neonatal birth weight were 37.1±1.2 weeks and 3.537±794 g, respectively. There were no stillbirths, perinatal infant deaths, or congenital malformations noted. There were two preterm births due to preeclampsia, one of whom had a low birth weight (1.800 g). We recorded one macrosomic baby (4.730 g). **Conclusion:** We observed that glycemic control improved with CSII therapy during pregnancy. We did not detect severe hypoglycemia or diabetic ketoacidosis in our research. In pregnant women with T1DM who had inadequate glycemic control with multiple daily insulin injection therapy, CSII might be a safe and appropriate treatment regimen.

Keywords: Type 1 diabetes mellitus; CSII, continuous subcutaneous insulin infusion; pregnancy; glycemic control

Özet

Amaç: Tip 1 diabetes mellituslu (T1DM) gebe kadınlarda fetal, maternal ve perinatal komplikasyon riski artmıştır. Bu raporda, T1DM'li gebelerde sürekli subkütan insülin infüzyonu [continuous subcutaneous insulin infusion (CSII)]nun gebelik sonuçları, glisemik kontrol ve akut komplikasyonlar üzerine etkilerini değerlendirmeyi amaçladık. **Gereç ve Yöntemler:** 2008-2014 yılları arasında kliniğimizde izlenen CSII tedavisi alan T1DM'li 15 kadının verileri retrospektif olarak incelendi. Akut komplikasyonlar, fetal/maternal ve perinatal komplikasyonlar ile glisemik kontrol analiz edildi. **Bulgular:** Hastaların ortalama yaşı 28,2±3,6 yıl, ortalama diyabet süresi ise 8±5,4 yıl idi. Gebelikleri sırasında şiddetli hipoglisemik atak ve diyabetik ketoasidoz izlenmedi. Gebeliğin 4-8. haftalarında ölçülen ortalama HbA1c, gebeliğin 34-38. haftalarında %7,4±1,3'ten %6,3±0,7'ye geriledi. Ortalama gebelik süresi ve yenidoğan doğum ağırlığı sırasıyla 37,1±1,2 hafta ve 3.537±794 g idi. Ölü doğum, perinatal bebek ölümü veya konjenital malformasyon görülmedi. Preeklampsi nedeni ile iki preterm doğum görüldü. Bu yenidoğanlardan biri düşük doğum ağırlığına (1.800 g) sahipti. Bir makrozomik bebek kaydedildi (4.730 g). **Sonuç:** Çalışmamızda gebelik sırasında CSII tedavisi ile glisemik kontrolde düzelme izlendi, şiddetli hipoglisemi veya diyabetik ketoasidoz saptanmadı. Günlük çoklu enjeksiyon (MDI) tedavisi ile glisemik kontrolü sağlanamayan T1DM'li gebe kadınlarda, CSII tedavisinin güvenli ve uygun bir tedavi rejimi olabileceği sonucuna vardık.

Anahtar kelimeler: Tip 1 diabetes mellitus; CSII, sürekli subkütan insülin infüzyonu; gebelik; glisemik kontrol

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Background

The incidence of pregnancies that are complicated with diabetes is increasing. Pregnancy complications are higher in type 1 diabetes mellitus (T1DM). In the present report, we aimed to evaluate the glycemic control parameters, acute complications, and pregnancy outcomes in T1DM pregnant women using continuous subcutaneous insulin infusion therapy (CSII).

Introduction

In addition to the high prevalence of diabetes, 1.5% of pregnancies are complicated with pregestational diabetes (1). Approximately half of the pregnancies with pregestational diabetes are affected by T1DM (2). Pregnant women with T1DM have an increased risk of fetal, maternal, and perinatal complications (3). The most common fetal adverse outcomes are perinatal loss (4-6), congenital malformations (7-10), fetal growth acceleration, and macrosomia (11,12). The most common maternal and gestational complications are abortus, premature delivery (13), preeclampsia (14,15), and worsening of retinopathy or nephropathy (4,5,13).

Moreover, the incidence of hypoglycemia and diabetic ketoacidosis is higher during pregnancy (16,17). Tight glycemic control at conception and during pregnancy is essential to optimize maternal and fetal outcomes. Strict glycemic targets can be achieved by intensive treatment regimens, such as CSII therapy or multiple daily insulin injections (MDI). Although some researchers in their guidelines have cautioned about the risk of ketoacidosis during CSII therapy, recent studies showed that CSII treatment is safe in pregnancy, and the metabolic control, maternal, fetal, and perinatal outcomes are similar in women treated with CSII therapy or MDI (18-20). We aimed to evaluate the effect of CSII therapy on metabolic control, acute complications, and pregnancy outcomes in pregnant T1DM women.

Material and Methods

This is a retrospective and observational report. The protocol was approved by the Gazi University Clinical Research Ethics Committee dated 28 November 2014 and no: 122761. The report followed the Declaration of Helsinki. The data of pregnant women with T1DM who had undergone CSII as intensive insulin therapy were analyzed. The patients were selected from our endocrinology clinic database between 2008 and 2014. Patients with incomplete records, diagnosed as type 2 DM and gestational DM, and those who were switched to CSII from MDI therapy after the first trimester, were excluded. After exclusion, we evaluated 15 pregnant women with T1DM. There were five patients who were already on CSII therapy. A total of 10 patients started CSII therapy at 4-8 weeks of pregnancy as they had frequent hypoglycemic or hyperglycemic episodes with MDI therapy. The age, duration of diabetes, duration of CSII, glycated hemoglobin (HbA1c), and body mass index (BMI) of the patients before parturition were recorded. The follow-up records were obtained every two or three weeks until the 30th week and henceforth, weekly until delivery. We initially measured HbA1c values by high-performance liquid chromatography (HPLC) followed by every 4 or 8 weeks. Severe hypoglycemic episodes, diabetic ketoacidosis, preeclampsia, and pregnancy-induced hypertension were recorded. The gestational hypertension was defined as blood pressure ≥140/90 mmHg after 20 weeks of gestation in a patient with previously normal blood pressure. We diagnosed preeclampsia if ≥300 mg protein in a 24-hour urine sample was detected in addition to pregnancy-induced hypertension. We also recorded weeks at delivery, perinatal mortality, stillbirth, congenital malformations, and birth weight. We defined stillbirth as a loss of fetus delivered after 20 completed weeks of gestation and perinatal death as a fetal death (stillbirth) or early neonatal death (the death of a newborn within the first seven days of life). Fetal macrosomia was defined as the birth weight ≥4500 g or higher than the 90th percentile. Low birth weight (LBW) was defined as the birth weight of a liveborn infant of ≤2500 g regardless of gestational age.

Statistical Analysis

We used SPSS 15 (Statistical Package for Social Sciences) program for statistical

analysis. Numeric variables are presented as mean±standard deviation. Descriptive statistics were performed for all variables.

Results

A total of 15 pregnant women with T1DM were included in the study. Of these patients, five were already on CSII therapy before pregnancy (mean duration of CSII treatment was 4±2.5 years), and 10 were switched to CSII from MDI therapy at 4-8 weeks of pregnancy due to frequent hypoglycemic and hyperglycemic episodes. The mean age of the patients was 28.2 ±3.6 years, and the mean duration of diabetes was 8±5.4 years. A total of three patients were using CSII with insulin lispro and one of them with insulin aspart. The others were on CSII therapy with regular insulin.

The mean HbA1c decreased from 7.4±1.3% (4-8 gestation weeks) to 6.3±0.7% (34-38 gestation weeks). The mean duration of pregnancy was 37.1±1.2 weeks. The mean neonatal birth weight was 3537±794 g. The mean daily insulin doses before delivery were 55.4±21.3 units, and the mean maternal weight gain was 13.9±4.7 kg during pregnancy (Table 1).

All patients gave birth by cesarean section. There were no congenital malformations, stillbirths, or perinatal infant deaths. Two of the preterm births occurred due to preeclampsia. The low birth weight was detected in an infant whose mother developed preeclampsia (1800 g). Neonatal jaundice and asphyxia were observed, in this newborn. There were no sequelae in this newborn. We did not observe diabetic ketoacidosis and severe hypoglycemic episodes during the pregnancies. We recorded one macrosomic baby with a weight of 4730 g. Neonatal hypoxia was not observed in this newborn. HbA1c of the mother was 8.4% in the first trimester and 7.5% in the third trimester. Her total daily insulin doses at delivery were 64 units (Table 2).

Table 1. Clinical characteristics and parameters of glycemic control of the subjects.

N:15	
Age (years)	28.2±3.6
Duration of diabetes (years)	8±5.4
HbA1c first trimester (%)	7.4±1.3
HbA1c third trimester (%)	6.3±0.7
Weeks at delivery	37.1±1.2
Birth weight (g)	3537±794
Maternal weight gain (kg)	13.9±4.7
Daily total insulin doses (U) before delivery	55.4±21.3

Variables are presented as mean ±standard deviation.

Discussion

To our knowledge, no prior studies from our country have examined CSII therapy in diabetic pregnant women. In our observation, there was a marked improvement in glycemic parameters in pregnant women with T1DM using CSII therapy. However, some patients' HbA1c values were higher than the target, which could be due to choosing a population with poor glycemic control under MDI therapy.

Pregnancy facilitates the development of ketoacidosis. However, we did not observe diabetic ketoacidosis or severe hypoglycemic episodes. Although some studies have reported a higher risk of ketoacidosis, improved metabolic control, and less severe hypoglycemia have been reported with CSII therapy (20,21). Some recent studies concluded that pregnancy outcomes and glycemic control were not significantly different between MDI or CSII therapy groups in T1DM. Giménez et al. compared CSII and MDI therapy in a total of 58 pregnant women with T1DM and reported that both the therapies were associated with similar results in metabolic control, maternal, fetal and perinatal outcomes (18). Wender-Ozegowska et al. reported decreased hypoglycemia and insulin requirement with the use of CSII therapy in pregnancies complicated with T1DM and similar pregnancy outcomes when compared with MDI (20). In another study, similar HbA1c values and metabolic control parameters were observed with CSII and MDI treatment (22). Zorić et al., in their study of a total of 17 newly diagnosed pregnant women with T1DM, reported that there was a significant improvement in HbA1c and the daily requirement for insulin during CSII therapy (23). The rate of fetal macrosomia in pregnant women with T1DM is reported between 20-54% in the literature (6,24,25). There is

Table 2. Clinical and metabolic characteristics of mothers and their infants.

Patient (N:15)	Age (years)	Duration of diabetes (years)	CSII pre-pregnancy	First trimester HbA1c (%)	HbA1c before delivery (%)	Weeks at delivery	Birth weight (g)
1.	35	13	+	8.90	7	38.3	2580
2.	29	5	-	7.4	5.2	38.3	4000
3.	27	17	+	8.1	6.4	37.6	3580
4.	25	13	+	8.4	7.50	37	4730
5.	28	10	+	7	5.7	37.6	4390
6.	28	1	-	7.3	6.3	36	3530
7.	31	13	-	6.6	6.1	38.2	3060
8.	29	1	-	5.9	6.6	38.2	3840
9.	28	13	+	7.4	5.5	36.4	3700
10.	33	6	-	6.4	6.8	35.1	3540*
11.	19	2	-	10.8	7.6	34.5	1800*
12.	26	8	-	8.4	6.1	37.2	3580
13.	27	4	-	5.90	5.4	38.2	3480
14.	29	6	-	6.9	6.5	38.2	2950
15.	30	8	-	6.4	5.9	37	4300

* Pregnancies complicated with preeclampsia.

an increased risk of up to four-folds in preeclampsia (24,25). In the present study, the rate of macrosomia and preeclampsia were consistent with the data in the literature.

Limitations

The limitations of the study were the lack of a control group and the sample size being small.

Conclusion

We conclude that CSII therapy may be a safe and appropriate treatment regimen in type 1 diabetic pregnant women.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Alev Eroğlu Altınova, Müjde Aktürk, Işılay Kalan Sarı; Design: Işılay Kalan Sarı, Müjde Aktürk; Control/Supervision: Müjde Aktürk, İlhan Yetkin, Nuri Çakır; Data Collection and/or Processing: Işılay Kalan Sarı, Çiğdem Özkan, Ceyla Konca Değertekin; Analysis and/or Interpretation: Işılay Kalan Sarı, Nuri Çakır, İlhan Yetkin; Literature Review: Ethem Turgay Cerit, Mehmet Muhittin Yalçın; Writing the Article: Işılay Kalan Sarı, Çiğdem Özkan, Alev Eroğlu Altınova; Critical Review: Ayhan Karakoç, Göksun Ayvaz; References and Fundings: Işılay Kalan Sarı, Alev Eroğlu Altınova, Ethem Turgay Cerit; Materials: Işılay Kalan Sarı, Çiğdem Özkan.

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