OBES SURG (2008) 18:1109–1111
DOI 10.1007/s11695-008-9544-5

RESEARCH ARTICLE

Pregnancy in Formerly Type 2 Diabetes Obese Women Following Biliopancreatic Diversion for Obesity

Gian Franco Adami · Federica Murelli · Lucia Briatore · Nicola Scopinaro

Received: 7 April 2008 / Accepted: 15 April 2008 / Published online: 14 May 2008

Abstract
Background This study describes the pregnancy of previously obese women with type 2 diabetic who reduced body weight and normalized serum glucose level following biliopancreatic diversion (BPD) for obesity.
Methods A subset of ten women who had type 2 diabetes prior to BPD and who developed pregnancy after the operation was retrospectively identified.
Results All pregnancies were completely normal, and serum glucose levels remained within the physiological range throughout all the pregnancy. These post-diabetic women delivered 13 infants in good health with a normal birth weight and no case of macrosomia.
Conclusions These data are a clinical confirmation of the post-BPD improvement of beta-cell response to increased functional demand in obese patients with preoperative type 2 diabetes.

Keywords Insulin function · Obesity · Obesity surgery · Pregnancy · Type 2 diabetes

Although in the second and third trimesters insulin resistance increases, during pregnancy, blood glucose values remain within the physiological range for a corresponding increase in insulin secretion [1]. On the contrary, in women with type 2 diabetes or with high-risk profile for diabetes, during pregnancy, the increase of beta cell secretion is not able to compensate for the increment of insulin resistance, resulting in hyperglycemia. Maternal hyperglycemia causes marked fetal hyperinsulinemia through inappropriate fetal pancreatic beta cell stimulation, macrosomia, increased congenital malformation, and both higher maternal and fetal complication rate compared with pregnancy in non-diabetic subjects [2–4], while better maternal glycemia control reduces perinatal morbidity and mortality [3, 4]. Therefore, in pregnant women with gestational diabetes, frequently, insulin treatment is needed with increasing insulin dose to compensate for insulin resistance and to maintain nearly normal glucose concentration.

This report describes the pregnancy of previously obese type 2 diabetic women who steadily reduced body weight and normalized serum glucose level following biliopancreatic diversion (BPD) for obesity.

Materials and Methods

Among the obese women who underwent BPD [5] at the Department of Surgery of the University of Genoa between 1976 and 2003, the subset of women with type 2 diabetes (serum glucose concentration ≥7 mmol/l) prior to BPD who developed pregnancy throughout the postoperative years was retrospectively identified. All the patients give their informed consent, and the study was approved by the local Ethical Committee. There were ten severely obese women with type 2 diabetes who underwent BPD at 24–38 (mean 30) years and developed 13 pregnancies following the operation at 28–41 (mean 34) years. Prior the operation, five of them have had type 2 diabetes lasting 1–3 years (three were treated with oral antidiabetic agents and two

No conflict of interest to disclose.

G. F. Adami (✉) · F. Murelli · N. Scopinaro
Dipartimento di Discipline Chirurgiche,
Facoltà di Medicina e Chirurgia, Università di Genova,
Genova, Italy
e-mail: adami@unige.it

L. Briatore
Dipartimento di Scienze Endocrine e Metaboliche,
Facoltà di Medicina e Chirurgia, Università di Genova,
Genova, Italy

Table 1 Ten formerly type 2 diabetes obese women who became pregnant after BPD and delivered 13 healthy infants

Name	Prior to BPD			BW at pregnancy	Weight gain	Serum glucose level throughout pregnancy					Birth weight
	Birth weight	BW	Glucose level			Pre	I trim	II trim	III trim	After delivery	
F.G.		142	11.6	61.2	3	4.3	3.3	3.5	4.7	3.9	2,830
D.M.	3,200	113	7.4	87	0.5	5.2	4.7	4.7	4.8	4.4	2,240
V.S.	4,500	115.5	11.0	70	7.5	5.3	5.0	4.2	4.2	4.5	2,710
M.P.	2,500	147.9	16.9	65	9	4.4	4.4	4.3	4.7	4.4	2,700
M.P.	2,500	147.9	16.9	69.5	4.5	4.8	3.7	4.3	5.0	4.8	2,500
F.C.	4,200	129	7.7	81	2	4.7	4.2	3.9	3.9	4.9	3,000
C.E.	4,500	129	7.4	83	3	4.0	4.0	4.9	4.3	4.7	2,560
P:C:		143	8.9	95	0	5.1	3.7	4.9	4.6	3.3	2,850
T.R.	4,150	120	7.9	83	6	4.3	4.4	4.4	4.6	4.8	3,330
T.R.	4,150	120	7.9	87	6	5.3	4.5	4.5	4.6	4.6	3,240
T.O.	3,500	109	7.0	73	3	4.5	4.4	4.4	4.5	4.2	2,800
M.A.	3,700	118	7.3	78	9.5	4.2	4.5	4.2	4.2	4.2	2,800
M.A:	3,700	118	7.3	74	8	4.2	3.9	4.5	4.2	3.9	3,150
Mean	3,691	126		79	4.4						2,823
SD	714	11.5		8.7	3.0						304

Anthropometric data (BW: body weight in kilograms and birth weight in grams) and serum glucose level (mmol/l) prior to BPD, at the pregnancy (pre), at the first (I trim), second (II trim), and third (III trim) trimesters, and after delivery

with diet alone), while in five of them the type 2 diabetes was diagnosed at the operation. Before BPD, the women of this subset had delivered 11 infants with a mean birth weight of 3823 g, six with a birth weight greater than 4 kg. After BPD, the women developed 13 pregnancies and delivered 13 singleton infants after a mean of 38 (range 32–42) weeks of gestation. After BPD, all the patients showed completely normal fasting serum glucose level at free diet and without medication. During the post-BPD pregnancy, the subjects were followed up as all pregnant women following BPD [6]. They were given nutritional advices in order to avoid protein malnutrition, and vitamins B_1, B_{12}, calcium, and folate supplementation. Serum glucose level was monthly determined, the diet was completely free, and no antidiabetic agent was used.

The information about pregnancy and delivery was obtained through direct or telephone interviews, office charts, and hospital records.

Results

Table 1 shows the anthropometric measures and the serum glucose levels observed prior to the operation, at pregnancy, throughout pregnancy, and at 1 year after delivery in formerly type 2 diabetes obese women. Before pregnancy, mean body weight was markedly lower than the preoperative, the values increased slightly during the pregnancy, and returned to levels substantially similar to the pre-pregnancy ones after delivery. While prior to BPD serum glucose levels were in the diabetic range, before pregnancy values were reduced within physiological level and in all patients remained quite unchanged in all trimesters and after delivery, values being below the 6 mmol/l limit in every determination at any time throughout pregnancy (Table 1). In all cases, pregnancy and delivery were uneventful (three operative delivery), and birth weight was substantially normal for the gestational age (in no cases above 3,500 g and in only one case below 2,500 g) at significantly lower (Wilcoxon $Z=-2.981$, $p=0.0029$) level than that of infants delivered by these women before BPD (Table 1).

Discussion

Following BPD, the improvement of insulin sensitivity is undoubtedly due to the weight reduction and to loss of body fat. However, the early normalization of serum glucose level suggests the action of some specific mechanisms, such as changes in the incretin pattern consequent to the exclusion of foregut, increased GLP-1 production due to food stimulation of distal small bowel, or lipid deprivation due to strongly reduced fat intestinal absorption [7, 8]. Furthermore, some recent studies have shown an increase in insulin secretion and beta cell sensitivity at short and at long term following BPD [9, 10]. In obese patients, type 2 diabetes mellitus results from increased insulin resistance and impaired beta-cell secretion; the reduction of peripheral insulin resistance with a concomitant enhancement of insulin secretion accounts for the recovery of glycemic homeostasis in nearly all type 2 diabetes obese patients submitted to BPD [11].

This is the first observation specifically focused on pregnancy in type 2 diabetes obese patients who normalized glucose metabolism after BPD. The pregnancy outcome for women with pre-existing type 2 diabetes is substantially worse than that of the general population [2] due to increased insulin requirement during the pregnancy and the consequent poor glucose homeostasis. On the contrary, in the post-diabetic women of this study, pregnancy was substantially normal in all cases without any specific therapy. Serum glucose level remained within physiological range throughout all the pregnancy at free diet and without antidiabetic medications. This suggests a highly satisfactory function of pancreatic beta cells that succeed in constantly maintaining the glucose homeostasis in spite of increased insulin requirement due to the pregnancy.

According to the Pedersen hypothesis, the impaired maternal beta-cell function and the poor glucose control result in a fetal hyperinsulinemia through inappropriate fetal pancreatic beta-cell stimulation, thus causing fetal macrosomia and most of the complications of diabetes in pregnancy [3, 4]. Prior to BPD, this subset of diabetic obese women delivered 11 heavy infants, six of them having a birth weight greater than 4 kg. Following BPD in the same woman, no maternal and neonatal complications or still-birth were observed, and all the infants showed a substantially normal birth weight for gestational age without any case of fetal macrosomia: the mean birth weight of infants conceived and delivered after BPD was markedly lower than that of babies previously conceived and delivered. These clinical data further support the complete recovery of beta cell function in post-diabetic subjects following BPD.

Previous studies have demonstrated that in obese patients with type 2 diabetes, BPD is able to induce a restoration of acute insulin response, thus indicating an enhancement towards normality of beta cell function [9, 10]. The clinical outcome of post-diabetic women who became pregnant following BPD supports the hypothesis that in obese subject with type 2 diabetes, the stable normalization of serum glucose following BPD is mainly accounted for by a recovery of beta cell function.

References

1. Catalano PM, Huston L, Amini SB, et al. Longitudinal changes in glucose metabolism during pregnancy in obese women with normal glucose tolerance and gestational diabetes mellitus. Am J Obstet Gynecol. 1999;180:903–16.
2. Dunne F, Brydon P, Smith K, et al. Pregnancy in women with Type 2 diabetes: 12 years outcome data 1990–2002. Diabet Med. 2003;20:734–8.
3. Walkinshaw SA. Pregnancy in women with pre-existing diabetes: management issues. Semin Fetal Neonatal Med. 2005; 10:307–15.
4. Pedersen J. The pregnant diabetic and her newborn—Problems and management. Copenhagen: Munksgaard; 1977.
5. Scopinaro N, Adami GF, Marinari UM, et al. Biliopancreatic diversion. World J Surg. 1999;22:936–46.
6. Friedman D, Cuneo S, Valenzano M, et al. Pregnancies in an 18-year follow-up after biliopancreatic diversion. Obes Surg. 1995;5:308–13.
7. Rubino F, Gagner M. Potential of surgery for curing type 2 diabetes mellitus. Ann Surg. 2002;236:554–9.
8. Greco AV, Mingrone G, Giancaterini A, et al. Insulin resistance in morbid obesity: reversal with intramyocellular fat depletion. Diabetes. 2002;51:144–51.
9. Polyzogopoulou EV, Kalfarentzos F, Vagenakis AG, et al. Restoration of euglycemia and normal acute insulin response to glucose in obese subjects with type 2 diabetes following bariatric surgery. Diabetes. 2003;52:1098–103.
10. Briatore L, Salani B, Andraghetti G, et al. Restoration of acute insulin response in T2DM subjects one month after biliopancreatic diversion. Obesity. 2008;16:77–81.
11. Scopinaro N, Marinari GM, Camerini GB, et al. Specific effects of biliopancreatic diversion on the major components of metabolic syndrome: a long-term follow-up study. Diabetes Care. 2005;28: 2406–11.