Use of Insulin Pumps in Pregnancies Complicated by Type 2 Diabetes and Gestational Diabetes in a Multiethnic Community

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OBJECTIVE — To describe the use of insulin pump therapy in women with gestational diabetes mellitus (GDM) or type 2 diabetes in pregnancy and persistent hyperglycemia despite multiple injections of subcutaneous insulin.

RESEARCH DESIGN AND METHODS — As part of a service audit, deliveries to women with diabetes at a single South Auckland hospital were reviewed from 1991 through 1994. Glycemic control was estimated by the mean of self-recorded and laboratory postprandial glucose concentrations. In a nested case-control study, pregnancies complicated by GDM/type 2 diabetes with use of an insulin pump were compared with those without insulin pump therapy and peak insulin requirements of 100–199 units/ day, matched for ethnicity and type of diabetes.

RESULTS — A total of 30 of 251 Polynesian, European, and South Asian women with singleton pregnancies complicated by insulin-requiring GDM/type 2 diabetes used an insulin pump. An additional two women with high insulin requirements discontinued pump therapy. None of the women with GDM/type 2 diabetes experienced severe hypoglycemia, whereas 79% of the women had improved glycemic control within 1–4 weeks. Mothers using a pump had greater insulin requirements (median maximum 246 vs. 130 units per day) and greater weight gain (10.6 vs. 5.0 kg). Their babies were more likely to be admitted to the Special Care Baby Unit but were neither significantly heavier nor experienced greater hypoglycemia than control subjects.

CONCLUSIONS — Insulin pump therapy seems to be safe and effective for maintaining glycemic control in pregnancies complicated by GDM/type 2 diabetes and requiring large doses of insulin.

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Gestational diabetes mellitus (GDM) is associated with important perinatal and long-term health risks for both mother and child (1). Type 2 diabetes in pregnancy is associated with an increased risk of operative delivery, and the risk of perinatal mortality may even be higher than that in type 1 diabetes (2). A study of women with GDM, in which a significant proportion had type 2 diabetes after pregnancy, clearly showed that tight glucose control, particularly of postprandial glucose, is associated with less neonatal hypoglycemia, macrosomia, and caesarean delivery (3). In that study, 88% of women achieved target glycemia using a three-times-per-day, split-evening-dose insulin regimen. Although reduced adherence to such regimens and dietary indiscretions can contribute to difficulties in glycemic control, some women need, but do not always receive, large amounts of insulin to achieve euglycemia. Achieving optimal glucose control is not always possible with a four-times-per-day insulin regimen.

New Zealand Polynesians (both indigenous Maori and those from the South Pacific) have a high prevalence of GDM (4), type 2 diabetes diagnosed at a young age (5), and obesity (6). Compared with European women with GDM, Polynesians with GDM are older, heavier, have worse hyperglycemia at diagnosis, are more likely to have type 2 diabetes postnatally, and are prone to worse perinatal outcomes (7). To address the difficulties in controlling hyperglycemia in Polynesian women, particularly with respect to the large volumes of insulin sometimes required for control, we introduced insulin pumps. We now describe the results of our experience over a 4-year period.

RESEARCH DESIGN AND METHODS

— Insulin pump therapy was used for women in whom a single dose of insulin at a given time exceeded 100 units, three premeal and one prebed injection failed to provide adequate glycemic control, or fetal growth remained accelerated despite optimal conventional insulin therapy. A standard approach was developed in 1990 with the introduction of Nipro pumps (Nipro, Osaka, Japan) for women with GDM or preexisting type 2 diabetes. This pump was simple to operate, had a manual setting of basal rates, and could deliver boluses. Table 1 shows the guideline used to begin pump therapy. Women with type 1 diabetes used more sophisticated pumps.

The insulin pump approach was used in the setting of a multidisciplinary Diabetes in Pregnancy clinic, including a di-

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Abbreviations: ADIPS, Australasian Diabetes in Pregnancy Society; GDM, gestational diabetes mellitus.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1—*Guideline for commencing pump therapy using U100 soluble insulin*

To calculate insulin requirements when changing from insulin injections to the pump, the following criteria were used as a baseline, although final amounts were tailored to the individual woman's needs (degree of persisting hyperglycemia, times of hypoglycemia, or euglycemia).

1. Total daily dose of insulin: if control has been suboptimal, the current daily dose of insulin should be used for the pump. When control has been relatively good, it is suggested that 80% of the present daily dose should be used.
2. To calculate the basal rate: approximately 44% of the total daily dose should be used for the basal insulin. This is divided into two basal rates as follows:
   - 80% for the daytime rate, which is usually from 7:00 A.M. to 7:00 P.M.
   - 20% for the nighttime rate, which would be from 7:00 A.M. to 7:00 P.M.
3. To calculate the bolus rates: the remaining 56% of the total daily rate is used for the boluses. Boluses are given 30 min before each meal and are calculated on a ratio of 5:3:4 for breakfast:lunch:dinner (e.g., for breakfast bolus multiple in sulin by 5/12).
4. Management of pump if hypoglycemia occurs: because the pump offered improved glycemic control, the risk of hypoglycemia is increased. It is important that the woman and her family understand clearly how to manage hypoglycemia. If blood glucose level is recorded at levels <4.0 mmol/l, the pump should be turned off and the hypoglycemia should be treated. Blood glucose levels should be monitored hourly, until they return to 4.0–4.5 mmol/l, and then the pump can be recommenced.
5. Initial follow-up: therapy is closely supervised by the diabetes midwifery educator initially on a daily basis by phone. Regular clinic visits continue. Insulin dosage is altered based on extent and pattern of hyperglycemia (19).

abetes midwifery educator who undertook home visiting, diabetes education (e.g., self glucose monitoring, insulin use, pump use), and much of the telephone stabilization (8). Women with GDM usually had been screened with a 50-g 1-h glucose challenge test. In 1993, the test and diagnostic criteria for GDM were changed from a 100-g 3-h test with the threshold for GDM being an area under the curve of 50 units (9) to the criteria set by the Australasian Diabetes in Pregnancy Society (ADIPS). This comprises a 75-g 2-h test, with a threshold of fasting glucose level of ≥5.5 mmol/l and/or a 2-h postprandial glucose level of ≥9.0 mmol/l (10).

The management of women with diabetes in pregnancy followed a standard approach (11), which was similar to the ADIPS guidelines (10) and the same (besides issues relating to oral medication) in GDM and type 2 diabetes. Clinic follow-up was performed monthly until 28 weeks' gestation, fortnightly until 36 weeks' gestation, and then weekly until term. Additional clinic visits were scheduled if they were believed to be clinically indicated. Insulin and any subsequent insulin pump therapy were started in the presence of inadequate glucose control, defined as ultrasonographic and/or clinical evidence of macrosomia and/or inadequately controlled glycemia (persistent fasting glucose ≥5.5 mmol/l or 2-h postprandial glucose ≥6.5 mmol/l or self blood glucose results increasing through the day) (11). All women receiving insulin were asked to perform self glucose monitoring up to five times per day, were given a 1,400- to 1,800-kcal diet (fewer calories for women with a BMI >29 km/m^2). Measures of long-term glycemic control were not routinely used, because HbA_{1c} was not then available and fructosamine was considered too unreliable. Pregnancies were allowed to go to term unless glycemic control had been inadequate or obstetric reasons for earlier delivery existed. Adjustments to the insulin dose were made both in the clinic and between clinics by the diabetes midwifery educator.

An audit program was undertaken between January 1991 and December 1994 to identify methods for improving care as previously described (7). Twin pregnancies, women delivering before 28 weeks, and women who did not receive insulin therapy have been excluded from the analyses. Glycemia was assessed by the mean of all laboratory 2-h postprandial glucose. Postnatal 75-g glucose tolerance testing among those with GDM was attempted, with a low response. Criteria for diagnosis were those in use at the time: diabetes if fasting glucose was ≥7.8 mmol/l and/or 2-h glucose was ≥11.1 mmol/l; and impaired glucose tolerance if 2-h glucose was 7.8–11.0 mmol/l. Neonatal hypoglycemia was defined as a neonatal heel-prick glucose level ≤1.6 mmol/l at any time). Insulin pumps were also used among four of seven European women and none of two Maori women with type 1 diabetes (i.e., 44.4% overall).

Statistics

All tests are two-tailed and were performed using SPSS-PC software (SPSS, Chicago, IL). Mean ± standard deviation or median (interquartile range) are shown. Continuous variables were compared using one-way analysis of variance and discrete variables using the χ^2 test. Statistical significance was taken at $P < 0.05$. The nested 1:2 case-control study was undertaken to women using insulin pumps with women of similar ethnicity, type of diabetes, and peak insulin dosage (where possible). All women who were not using an insulin pump, with preexisting tablet-treated type 2 diabetes or with peak insulin requirements higher than 200 units per day, were included as control subjects. The remaining 40 control subjects were randomly selected from the European, South Asian, and Polynesian women with GDM, peak insulin requirements of 101–199 units per day, who had not received an insulin pump. The study was undertaken as a service audit and was approved by local management.

RESULTS — Insulin pumps were used in 1 of 27 (3.7%) European woman, 7 of 56 (12.5%) Maori women, 21 of 151 (13.9%) Pacific Islands women, and 1 of 17 (5.9%) South Asian women. None of the 10 "other" Asian women required an insulin pump. Among Europeans, Polynesians, and South Asians, there were 251 singleton pregnancies of 28 weeks' gestation or more in which insulin was required, as shown in Table 2. Pump therapy was used continuously in 30 pregnancies (12.0%), although in an additional two women, insulin pump therapy was started and then discontinued, because the patients preferred to continue with the multiple injection regimen (6.7% failure rate). Women on insulin or tablet therapy for preexisting diabetes were significantly more likely to require an insulin pump during pregnancy ($P < 0.001$) (Table 1).

Table 2—*Use of insulin pump, peak insulin dosage, and type of diabetes among European, Polynesian, and South Asian patients*

	On pump	Not on pump
Number of deliveries*	30	221
Peak insulin dosage		
1–100 units/day	0%	63.0%
101–200 units/day	31.0%	34.1%
>200 units/day	69.0%	2.9%
Type of diabetes		
Preexisting insulin-treated type 2 diabetes	50.0% (5/10)	
Preexisting tablet-treated type 2 diabetes	33.3% (5/15)	
Preexisting diet-treated type 2 diabetes	0% (0/6)	
GDM	9.1% (20/220)	

*A total of 23 women used the pump once during their only pregnancy in the series, 5 women used the pump during one of two pregnancies, and 1 woman used the pump in two of two pregnancies. A total of 29 women used an insulin pump at least once, and 214 women never continuously used a pump (2 began to use the pump and stopped).

Among women with GDM/type 2 diabetes, there were no significant ethnic differences in use of insulin pumps within diabetes type. Access to insulin pumps was limited (up to five were available for use), and a small number of women with peak insulin requirements >200 units per day were not able to use the pumps. None of the women using an insulin pump experienced a hypoglycemic episode during which assistance was required. Detailed glycemic data for each clinic were available for deliveries that occurred in 1993 and 1994. In the 14 women treated with an insulin pump for whom results of self glucose monitoring before and after initiation of pump therapy were available, an improvement in glycemic control was demonstrable by the next clinic visit (1–2 weeks) in 79%, within 4 weeks in 14%, and within 6 weeks in the remainder. Mean glycemia decreased from 6.6 ± 1.3 to 5.3 ± 0.6 mmol/l. In the women in whom 2-h postprandial glucose was recorded before and after pump therapy, mean glycemia decreased from 9.8 ± 3.6 to 5.6 ± 2.1 mmol/l.

Table 3 shows the results of the nested case-control study. Control subjects and case subjects were well matched for ethnicity, age, and type of diabetes. Those using insulin pumps had booked earlier, had higher fasting hyperglycemia (if GDM), used more insulin, put on more weight and were more likely to have babies admitted to the Special Care Baby Unit. However, birth weight and neonatal hypoglycemia rates were similar. Caesarean section and postnatal abnormal glucose tolerance rates (among those with GDM) were not significantly higher among those on pumps. A similar number of babies weighed <3,000 g at birth (10.2 and 11.8%, respectively).

CONCLUSIONS — Insulin pumps have often been used in pregnant women with type 1 diabetes with good effects (12–14). Use in GDM and type 2 diabetes has not hitherto been described, although use of insulin pumps according to the criteria defined here is logical. Our series confirms that insulin pump therapy in type 2 diabetes and GDM is well tolerated. Such therapy is associated with no significant hypoglycemia, and control of hyperglycemia is achieved to a level unlikely with large boluses of subcutaneous injections of insulin. Perinatal outcomes were comparable to those in women with less hyperglycemia and lower insulin requirements. However, use of insulin pumps was associated with substantial weight gain and a greater likelihood of admission to the Special Care Baby Unit. Whether the latter was related to the "worse" diabetes status among the pump users or pump therapy itself remains unknown.

Table 3—*Nested case-control study*

	Pump user	Not pump user	Significance
Number of deliveries	30	60	
GDM (*n*)	66.7% (20)	75.0% (45)	0.486
Ethnicity (European, Maori, Pacific Islands, South Asian)	1, 7, 21, 1	1, 15, 41, 3	0.939
Age (years)	32 ± 5	33 ± 7	0.896
Smoker	20.0%	23.3%	0.720
Prior diabetes in pregnancy	63.3%	55.0%	0.451
High blood pressure	16.7%	11.7%	0.511
Parity	3 ± 2	3 ± 2	0.216
Gestation at booking (weeks)	15 ± 7	19 ± 8	0.009
Weight at booking (lb)	99.4 ± 18.6	95.9 ± 15.8	0.345
Diagnostic fasting glucose	7.6 ± 1.6 (16)	6.8 ± 1.6 (41)	0.105
Maternal weight gain from booking	12.1 ± 8.9	8.1 ± 6.0	0.014
Mean 2-h postprandial glucose (mmol/l)	6.6 ± 1.8	6.4 ± 1.6	0.550
Maternal weight gain from referral (kg)	10.6 ± 8.8	5.0 ± 4.9	0.000
Maximum insulin dose (units)			
Median (range)	246 (116–501)	130 (48–288)	0.000
Weight (units/kg) at booking	2.68 ± 1.10	1.52 ± 0.50	0.000
Gestation at delivery	39 ± 2	39 ± 2	0.282
Induction	50.0%	44.1%	0.695
Admitted to Special Care Baby Unit	56.3%	25.0%	0.033
Length of stay in Special Care Baby Unit (days)	2 (0–13)	2 (0–4)	0.303
Neonatal hypoglycemia ≤1.6 mmol/l	26.7%	19.6%	0.454
Big baby (4+ kg)	34.4%	40.0%	0.803
Caesarean section (Booked and emergency)	40.0%	28.8%	0.287
Emergency	30.0%	15.0%	
Booked	10.0%	13.3%	
Fetal 1-h glucose	2.5 ± 1.3	2.6 ± 1.2	0.844
Birth weight	3,790 ± 730	3,720 ± 790	0.704
Abnormal glucose tolerance test 6 weeks postpartum (*n*, GDM only)	28.6% (7)	8.3% (12)	0.243

Unless otherwise indicated, data are *n*, means ± SEM, means ± SEM (*n*), or mean (range).

The comparable median length of stay in the Special Care Baby Unit of 2 days in both groups suggests that indications for admission were serious enough to require overnight admission in most cases. Diabetic ketoacidosis among pump users is, of course, not an issue among these women. Although minor infections at the site of the cannula did occur, none of these required discontinuation of pump therapy. The availability of a diabetes midwifery educator contributed significantly to the ability to rapidly adjust insulin therapy between clinic visits (8).

We have focused on ambient glycemia to reduce the risk of perinatal morbidity, and our findings do not suggest that such massive doses of insulin cause harm. Although we have used large amounts of insulin, others have also used more than 100 units per day on average (3,15). Attempting to balance the real risk of maternal hyperglycemia against a hypothetical risk from hyperinsulinemia is an area in which further evidence would be helpful. No harmful effects have been proposed, although downregulation of the insulin receptor and the generation of insulin antibodies are putative risks. However, definitive demonstration of benefits and cost-effectiveness of insulin therapy in GDM and type 2 diabetes clearly requires a randomized trial. Our experience was initiated as a result of the special nature of practice in South Auckland, with its large numbers of Polynesians and the high prevalence of obesity and obesity-driven hyperinsulinemia (6). Few Europeans or South Asians and no other Asians with either GDM or type 2 diabetes required insulin pump therapy; therefore, demand for such high doses of insulin in other countries is likely to be limited. Availability of U500 insulin was sporadic at the time and not used among the pregnancies reported here. As evidence emerges on the long-term safety of metformin use in pregnancy, this may also increasingly be considered as an option instead of (or in addition to) insulin therapy. Our study, and indeed our clinical practice, was hampered by the lack of quality measures of hyperglycemia. We used a mix of laboratory fasting and postprandial glucose measures and self glucose monitoring. At the time, the latter consisted of either visual strips or increasingly some of the earlier nonmemory glucose reflectance meters. The latter were known to be associated with accuracy problems (16). Although we used the mean results of glucose monitoring tests, problems with precision and reporting were frequently demonstrated by inconsistencies between laboratory and self glucose monitoring results. The use of HbA_{1c} was not available at the time (and indeed would have changed too slowly to guide the changes in insulin therapy), and fructosamine was believed to be too unpredictable to be of use (10).

The long-term impact of the improvement in glycemia before and after the introduction of the insulin pump is unknown. Previously, in a predominantly Polynesian sample, we have shown less adiposity in the offspring of women with GDM who were treated with insulin compared with the offspring of those who were treated only with diet (17). We have also previously found that maternal obesity is associated with both mild hyperglycemia and fetal hyperinsulinemia (18,19), supporting the hypothesis that even mild hyperglycemia can be associated with fetal hyperinsulinism and perhaps can increase the risk of diabetes and obesity in the offspring over the longer term. A follow-up study of the offspring would clearly be an important limb of any randomized trail.

In conclusion, we have shown that the use of insulin pumps in women with GDM and type 2 diabetes during pregnancy is a safe and potentially useful approach for those women with high insulin requirements whose glycemic targets are not being achieved. This should be of particular interest in countries with large Polynesian communities and other groups requiring large amounts of insulin to achieve euglycemia.

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