Diabetologia (2011) 54:2466–2467
DOI 10.1007/s00125-011-2256-8

LETTER

Could there be a role for metformin in type 1 and type 2 diabetic pregnancies?

I. Pernicova · M. J. Prasai · E. J. Close · K. Drury · S. G. Gilbey · J. A. Brewster · E. M. Scott

Received: 23 May 2011 / Accepted: 29 June 2011 / Published online: 16 July 2011

Keywords Metformin · Obesity · Pregnancy · Type 1 diabetes · Type 2 diabetes

To the Editor: We read with interest the systematic review by Vella et al. on the use of metformin in type 1 diabetes, which concludes that metformin therapy is associated with lower insulin requirements in that disease [1]. Given the current epidemic of obesity, this is highly relevant because insulin sparing in the treatment of type 1 diabetes may also attenuate weight gain, as shown in several small studies not included in the formal meta-analysis [2].

Maternal obesity is rising. It is associated with a higher risk of fetal and maternal complications, and is an indicator of midlife obesity [3]. Pregnancy is associated with increased insulin resistance, and high maternal insulin secretion promotes maternal gestational weight gain and weight retention post-partum [4]. In gestational diabetes, the use of metformin has been associated with less weight gain in pregnancy without increased adverse outcomes [5, 6]. The effect of metformin on weight gain in pregnant women with pre-existing diabetes is unknown.

Metformin is not licensed for use in pregnancy. However, in view of growing supportive evidence, the National Institute for Health and Clinical Excellence (NICE), the UK body responsible for national guidelines on clinical practice, approved its use in 2008. Our practice changed then from solely using insulin to continuation of metformin in pregnant women with type 2 diabetes.

We performed a case note review of 56 consecutive pregnancies with pre-existing diabetes (2006 to 2010) from our clinic. The aim was to examine the extent of maternal weight gain and the effect of metformin use, with an emphasis on weight pre-pregnancy and at 6 months post-partum. Of the women included, 17 had type 2 diabetes treated with insulin alone during pregnancy, 17 had type 2 diabetes and received metformin with or without insulin (three of whom received metformin alone throughout pregnancy, with 14 requiring addition of insulin to metformin to meet their glycaemic targets) and 22 had type 1 diabetes treated with insulin. There was no statistical difference in baseline characteristics (ethnicity, age, duration of diabetes, parity, delivery week, HbA_{1c}, BMI, pre-pregnancy treatment and insulin dose) among the type 2 diabetic women, nor was there any difference in post-partum management and follow-up. The women in our review with type 1 diabetes were younger, had longer diabetes duration and were less heavy. Glycaemic control was comparable.

The BMI (kg/m^2) of the type 2 diabetic women changed from 33.4 pre-partum to 37.0 post-partum in the insulin alone group vs 34.3 to 34.2 in those receiving metformin and 24.9 to 26.5 in women with type 1 diabetes ($p<0.0001$). This corresponded to a mean weight retention

I. Pernicova (✉) · E. J. Close · K. Drury · S. G. Gilbey · E. M. Scott
Department of Diabetes and Endocrinology,
Manny Cussins Centre, St James University Hospital,
Beckett Wing,
Leeds LS9 7TF, UK
e-mail: idaper@seznam.cz

I. Pernicova · M. J. Prasai · E. M. Scott
Leeds Institute of Genetics Health and Therapeutics,
University of Leeds,
Leeds, UK

J. A. Brewster
Department of Obstetrics and Gynaecology,
Leeds Teaching Hospitals,
Leeds, UK

post-partum of 11% (~10 kg) in type 2 diabetic women treated with insulin alone, 0% in type 2 diabetic women treated with metformin with or without insulin, and 7% (~4 kg) weight gain in women with type 1 diabetes ($p<0.0001$). This contrasts with previously reported 6 months post-partum weight retention of 1.3–1.7 kg in the general population [7]. Of the women studied, 47% of those with type 2 diabetes treated solely with insulin, none of those who continued metformin and 23% of those with type 1 diabetes retained more than 9 kg ($p=0.005$). This compares with 1.7% of women from the general population according to previous publications [8]. In addition, 41% of the women who continued metformin throughout pregnancy were lighter than pre-pregnancy at 6 months post-partum vs none of those with type 2 diabetes treated by insulin alone ($p=0.007$). Women taking metformin had lower insulin requirements by 46% at delivery ($p=0.04$). There were no statistically significant differences in maternal and neonatal outcomes between the groups.

Our data show that being overweight at the start of pregnancy and post-partum weight retention constitute a substantial problem not only in women with type 2 diabetes, but also in those with type 1 diabetes. The development of strategies to combat this is crucial. In our routine clinical practice metformin is highly effective in aiding weight management in pregnancy in women with type 2 diabetes. Although in our study the women with type 2 diabetes were heavier at the start of pregnancy than their type 1 diabetic counterparts, type 2 diabetic women receiving metformin during pregnancy retained substantially less weight post-partum. The long-term effects on offspring of maternal metformin use during pregnancy are unknown. Moreover, there have been concerns regarding an increased propensity to hypoglycaemia in type 1 diabetic patients treated with metformin [2]. Nevertheless, we suggest that there may be a role for metformin in selected obese women with type 1 diabetes in pregnancy. Further studies are needed to explore and to validate this question. Our findings offer a promising opening.

Duality of interest The authors declare that there is no duality of interest associated with this manuscript.

Contribution statement All authors contributed to the conception and design, data collection, analysis and interpretation of the results, drafting and revision of the article, and the approval of its final version.

References

1. Vella S, Buetow L, Royle P, Livingstone S, Colhoun HM, Petrie JR (2010) The use of metformin in type 1 diabetes: a systematic review of efficacy. Diabetologia 53:809–820
2. Lund SS, Tarnow L, Astrup AS et al (2008) Effect of adjunct metformin treatment in patients with type-1 diabetes and persistent inadequate glycaemic control. A randomized study. PLoS One 3:e3363
3. Melzer K, Schutz Y (2010) Pre-pregnancy and pregnancy predictors of obesity. Int J Obes (Lond) 34(Suppl 2):S44–S52
4. Scholl TO, Chen X (2002) Insulin and the "thrifty" woman: the influence of insulin during pregnancy on gestational weight gain and postpartum weight retention. Matern Child Health J 6:255–261
5. Balani J, Hyer SL, Rodin DA, Shehata H (2009) Pregnancy outcomes in women with gestational diabetes treated with metformin or insulin: a case–control study. Diabet Med 26:798–802
6. Rowan JA, Hague WM, Gao WZ, Battin MR, Moore MP (2008) Metformin vs insulin for the treatment of gestational diabetes. N Engl J Med 358:2003–2015
7. Amorim AR, Rossner S, Neovius M, Lourenco PM, Linne Y (2007) Does excess pregnancy weight gain constitute a major risk for increasing long-term BMI? Obesity (Silver Spring) 15:1278–1286
8. Greene GW, Smiciklas-Wright H, Scholl TO, Karp RJ (1988) Postpartum weight change: how much of the weight gained in pregnancy will be lost after delivery? Obstet Gynecol 71:701–707