# **Gestational diabetes therapy:**

## Right person, right treatment, 'night' time.

## Authors:, Eleanor M Scott<sup>1,2</sup>Alia Alnaji<sup>1</sup>, Lina Alrefaii<sup>1</sup>, Del Endersby<sup>2</sup>, Sarah J Cartland<sup>1,2</sup>, Stephen G Gilbey<sup>3</sup>, Paul E Jennings<sup>4</sup> Helen R Murphy<sup>5</sup>, Graham R Law<sup>1</sup> Eleanor M Scott<sup>2,3</sup>

- (1) School of Health and Social Care, University of Lincoln, UK.
- (2) Division of Clinical and Population Sciences, Leeds Institute of Cardiovascular and Metabolic Medicine, University of Leeds, UK
- (3) Leeds Teaching Hospitals NHS Trust, Leeds, UK
- (4) York NHS Foundation Trust, York, UK
- (5) Division of Maternal Health, St Thomas's Hospital, Kings College London, UK

**Corresponding author:** Dr Eleanor M Scott, LIGHT Laboratories, Level 7, Clarendon Way, University of Leeds, Leeds, LS2 9JT; Tel: +44 (0)113 3437762; E-mail: e.m.scott@leeds.ac.uk

Word Count: 426

#### **References:** 5

**Funding:** G.R.L. and E.M.S. were funded by the Higher Education Funding Council for England. H.R.M. was funded by the National Institute for Health Research (CDF-2013-06-035). L.A. was funded by a University of Leeds International Studentship. A.A. was funded by the Saudi Arabian Government.

**Duality of Interest.** E.M.S. serves on the Abbott Diabetes Care Global Advisory Paneland has received honoraria. H.R.M. serves on the Medtronic European Scientific Advisory Board. No other potential conflicts of interest relevant to this article were reported. We thank Foussard et al for their insightful comments (1) on our recent paper (2). We demonstrated that women with gestational diabetes who subsequently have a large for gestational age infant (LGA), run significantly higher glucose overnight, detectable by continuous glucose monitoring (CGM), at 32 weeks gestation than those women who do not go on to have LGA (2). We speculate that there may be several reasons why this is observed.

Foussard et al (1) suggest that irrespective of the cause, NPH insulin administered in the evening, should be considered the treatment of choice due to its peak action coinciding with the relative nocturnal hyperglycemia we demonstrated. Our own clinical practice has been to use a long acting insulin analogue (e.g. detemir or glargine) overnight to target a raised fasting self-monitored blood glucose (SMBG), and quick acting analogue insulin with meals to specifically target 1hr postprandial SMBG.

None of the women in the current study were therefore treated with NPH insulin, so we are unable to evaluate Foussard's valid hypothesis regarding the potential efficacy of NPH at targeting nocturnal hyperglycemia. It is worth noting that in our study, fewer women in the LGA group were being treated with insulin (n=1; 7%) at the time of CGM, compared to the women who subsequently didn't have LGA (n=20; 14%). There were similar numbers of women with and without an LGA infant on Metformin (57% vs 54%). Although we are clearly underpowered to draw definitive conclusions, this perhaps suggests that long acting analogue insulin was effective at preventing a higher glucose overnight.

The effects of different insulin on glucose control and outcomes have been studied in pregnancies affected by diabetes. It is interesting that in GDM and T2DM pregnancies when NPH and detemir are compared NPH is associated with more hypoglycaemia (3). In T1DM pregnancy detemir has been shown to be more effective at lowering fasting SMBG than NPH (4), and when detemir and glargine have been compared then glargine is associated with a lower prevalence of LGA in T1DM, with no difference observed in glucose control (5). None of these studies included CGM and whilst their impact on nocturnal glucose control alone cannot be specifically addressed they illustrate that the effect of any insulin needs to be considered in the context of managing the whole pregnancy.

We believe the real challenge lies not in which treatment to choose, but in detecting the need for additional treatment in the first place. Only then can we personalise therapy to the glucose profile in the right woman at the right time.

### References

1) Foussard N Cambos S, Poupon P, Monlun M, Blance L, Haisaguerre M, Grouthier V, Velayoudom-Cephise FMohammedi K, Rigalleaue V. Nocturnal hyperglycaemia in Gestational Diabetes Mellitus: Which second-line therapy? Comment on: Law and al.Suboptimal Nocturnal Glucose Control Is Associated With Large for Gestational Age in Treated Gestational Diabetes Mellitus. Diabetes Care 2019 in press

2) Law GR, Alnaji A, Alrefaii L, Endersby D, Cartland SJ, Gilbey SG, Jennings PE, Murphy HR, Scott EM. Suboptimal nocturnal glucose control is associated with large for gestational age in treated gestational diabetes. Diabetes Care 2019 in press

3) Herrera KM, Rosenn BM, Foroutan J, Bimson BE, Al Ibraheemi Z, Moshier EL, Brustman LE. Randomized controlled trial of insulin detemir versus NPH for the treatment of pregnant women with diabetes. Am J Obstet Gynecol. 2015;213(3):426.

4) Mathiesen ER, Hod M, Ivanisevic M, Duran Garcia S, Brøndsted L, Jovanovic L, Damm P, McCance DR; Detemir in Pregnancy Study Group. Maternal efficacy and safety outcomes in a randomized, controlled trial comparing insulin detemir with NPH insulin in 310 pregnant women with type 1 diabetes. Diabetes Care. 2012;35(10):2012-7.

5) Callesen NF, Damm J, Mathiesen JM, Ringholm L, Damm P, Mathiesen ER. Treatment with the long-acting insulin analogues detemir or glargine during pregnancy in women with type 1 diabetes: comparison of glycaemic control and pregnancy outcome. J Matern Fetal Neonatal Med. 2013;26(6):588-92.