Improving pregnancy outcome in obese women: the UK Pregnancies Better Eating and Activity randomised controlled Trial

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†In memoriam

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Scientific summary

The UPBEAT trial

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Scientific summary

Background

The increasing prevalence of obesity in UK women of reproductive age has implications for obstetric practice. Obesity in pregnancy is associated with, among other things, heightened risk of gestational diabetes mellitus (GDM), pre-eclampsia, thromboembolism, dysfunctional labour, delivery by caesarean section, postcaesarean wound infection and postpartum haemorrhage and lower rates of breastfeeding. Pregnancy in all women leads to a degree of insulin resistance, which is exaggerated in obese women, in whom aberrant glucose homeostasis may lead to GDM. Maternal glycaemia, through stimulation of fetal hyperinsulinaemia, leads to fetal macrosomia even in mothers who are not overtly diabetic, leading to an increased risk of stillbirth and complications at the time of delivery. The high rates of caesarean section, increased hospital admissions, greater length of stay and neonatal intensive care are associated with substantive NHS costs. There is no evidence-based intervention that improves pregnancy outcome in obese pregnant women. Considerable effort has been directed towards prevention of gestational weight gain (GWG) through 'healthy' dietary advice, but none has been shown to prevent adverse outcomes. The hypothesis addressed in this study was that a behavioural intervention that focused on reducing maternal insulin resistance rather than weight gain would lead to prevention of GDM, and that this would reduce the risk of large-for-gestational-age (LGA) infant deliveries, thereby offering an alternative strategy to limitation of GWG. The strategy was to use established behavioural change principles adapted for use in pregnancy to deliver a complex intervention comprising recommendations for a low-glycaemic index diet, reduced saturated fat intake and increased physical activity (PA), all of which have been associated with improved insulin sensitivity.

Objectives

The aim of this research programme was to develop, pilot and test in a randomised controlled trial (RCT) a novel behavioural (diet and PA) intervention in obese pregnant women. The main objectives were:

1. to determine in a development phase, following a review of the relevant literature, the best approach and delivery for the proposed intervention, develop and standardise the content and delivery method and assess feasibility and acceptability to women and providers with a view to optimising the intervention for use in a pilot trial.
2. to undertake a pilot trial to establish the efficacy of the intervention in changing dietary and PA behaviours, and to evaluate all practical aspects of delivering the intervention.
3. to undertake a RCT to determine whether or not the intervention reduces the risk of GDM in obese pregnant women and the number of LGA infant deliveries.

Methods

The complex intervention was evaluated in accord with the UK Medical Research Council Framework for the development and evaluation of complex interventions, delineated by three phases as described in *Objectives*. As interventions can be informed by understanding the intentions of pregnant women to change dietary behaviours a questionnaire-based study was undertaken in 103 pregnant women to appraise their intentions or perceived barriers to changing their diet in pregnancy to include the foods targeted by the UK Pregnancies Better Eating and Activity Trial (UPBEAT) intervention. A study was also performed to assess whether or not pedometers could provide an inexpensive assessment of PA for women in the pilot and main RCT to enable determination of the effect of the intervention on PA. A multidisciplinary team of a social scientist, a

psychologist, nutritionists, a physiologist, an obstetrician and a senior midwife developed the intervention, which was delivered by a health trainer (HT). The UPBEAT intervention comprised an initial one-to-one session followed by eight weekly sessions delivered in groups or individually, and was informed by psychological models of health behaviour including control theory and social cognitive theory. Specific, measurable, achievable, relevant and time-specific (SMART) diet and activity goals were set each week. For those women unable to attend, the session content was delivered by telephone or e-mail. A pilot trial to assess delivery and acceptability of the intervention, and to determine whether or not diet and PA were changed by the intervention, was undertaken in 183 obese pregnant women randomised to standard antenatal care or to the intervention superimposed on standard antenatal care. Further analyses of the pilot study included a study of baseline biomarkers and clinical risk factors as potential predictors of GDM, and a study of PA and pregnancy outcomes. The pilot trial led to a RCT of the intervention in 1555 obese pregnant women from antenatal populations of eight inner-city UK hospitals. Women were randomised to the intervention between 15^{+0} and 18^{+6} weeks' gestation. The primary outcome of the RCT for the mother was GDM [as measured by the International Association of the Diabetes and Pregnancy Study Groups (IADPSG)'s diagnostic criteria] and for the infant, LGA delivery (i.e. customised birthweight $\geq$ 90th centile for gestational age).

In an economic evaluation, a within-trial cost–utility analysis was undertaken to estimate the cost-effectiveness of the health training (intervention) over and above standard care (control). The items of resource assessed were contacts to provide the health training intervention, antenatal admissions, cessation of pregnancy and postnatal admissions.

Results

Phase 1: development phase

This phase of the study led to development of the intervention as described in the *Background* section above. The questionnaire-based study of pregnant women's ($n = 103$) intentions to adopt the dietary recommendations identified by the intervention (reduced intake of high-sugar and high-fat foods and increased fruit and vegetable consumption) found that perceived benefits for the health of the mother and baby provided the strongest incentive for intentions of eating the target foods, whereas barriers to change appeared to be discounted in pregnancy. This study informed the delivery of the intervention by the HTs, as it suggested dietary interventions in pregnant women should emphasise health benefits for the mother and child rather than focusing on barriers to change. A comparison in 58 overweight and obese women between assessment of PA using a pedometer (CW701 Digi-Walker™ Pedometer; Yamax, Bridgnorth, UK) step counts and an accelerometer (GT1M; ActiGraph, Pensacola, FL, USA) showed that there was poor agreement between the two. It was concluded that accurate assessment of PA in the pilot study would be best undertaken using an accelerometer as well as a validated questionnaire.

Phase 2: pilot trial

In total, 183 women [mean body mass index (BMI) of 36.3 kg/m^2] consented to participate in a pilot RCT of the UPBEAT intervention and 473 eligible women declined to participate. Dietary assessment by a triple-pass 24-hour recall demonstrated that women in the intervention arm demonstrated a significant reduction in dietary glycaemic load (GL) between recruitment and 28 weeks' gestation [–33 points, 95% confidence interval (CI) –47 to –20 points] compared with women in the standard care arm. Objectively measured PA (by accelerometry) was not different between control and intervention arms, whereas women in the intervention arm self-reported an increase in walking for leisure (14 minutes, 95% CI 5 to 23 minutes). This level of activity may not have been adequately captured by accelerometry, being a low-level activity, but could have also reflected reporting bias. Process evaluation identified that the dietary advice was well received by the participants and confirmed the results of the PA data which suggested that changes in PA data were more difficult to achieve. Identification of barriers to recruitment, HT session attendance and compliance led to modification of the intervention delivery but not to any change in the intervention per se. The incidence of GDM (30% by IADPSG's diagnostic criteria) in the pilot trial informed the sample size for the RCT, powered for a 25% reduction in GDM (1546 women).

An investigation of prediction of GDM in 106 of the pilot trial participants, of whom 27.4% developed GDM, identified age, parity, diastolic blood pressure and black ethnicity to be associated with later development of GDM. The area under the receiver operator characteristic curve for clinical risk factors alone (0.760), increased significantly with the addition of adiponectin (0.834, $\chi^2 = 4.00$; $p = 0.046$) measured at recruitment (early second trimester).

An investigation of the association between PA and pregnancy outcomes was undertaken among the 183 pilot trial participants. As no difference in objectively measured activity was observed between women in standard care and intervention arms, light-intensity PA was lower in early pregnancy in women who delivered macrosomic infants. Maternal sedentary time at 35–36 weeks' gestation was positively associated with neonatal abdominal circumference, and moderate-intensity PA was inversely related to neonatal abdominal circumference. This suggested that PA is an appropriate target for interventions to improve infant outcomes.

Phase 3: the UK Pregnancies Better Eating and Activity trial randomised controlled trial

Following report of the pilot trial to the National Institute for Health Research (NIHR), agreement to continue recruiting to the RCT was provided. In total, 1555 obese pregnant women (mean BMI of 36.3 kg/m^2) were recruited to the trial. Analysis was by intention to treat. The incidence of GDM was 26% in the standard care group and 25% in the intervention group (risk ratio 0.96, 95% CI 0.79 to 1.16; $p = 0.68$). Eight per cent of infants were LGA in the standard care group, compared with 9% in the intervention group (risk ratio 1.15, 95% CI 0.83 to 1.59; $p = 0.40$). Therefore, the intervention did not reduce GDM in pregnant obese mothers or deliveries of LGA infants, despite a significant reduction in the dietary GL ($p < 0.001$), carbohydrate intake ($p < 0.001$) and saturated fat intake ($p < 0.001$), and an increase in fibre uptake ($p = 0.013$) and PA (walking, minutes/week, $p = 0.0018$), together with a 0.55-kg reduction in GWG ($p = 0.041$) and lower maternal sum of skinfold thicknesses ($p = 0.0081$). There was no reduction in any other clinical pregnancy outcome of relevance in either the mother or the infant (secondary outcomes). The number of LGA infants being born in all trial participants was lower than expected; we suggested this could have arisen from universal screening for GDM in mothers using IADPSG's criteria and appropriate treatment following diagnosis.

Conclusions

A theoretically based intensive complex intervention combining dietary and PA advice to reduce GDM in obese pregnant women and the number of LGA infant deliveries was developed, in accordance with Medical Research Council guidelines, in three phases. The first, the development phase, provided useful information on relationships between current dietary behaviours and intentions to change behaviours as well as health incentives that could help delivery of the intervention. This phase also enabled assessment of appropriate measures for objective assessment of PA, and the importance of determining whether or not an intervention changes behaviours in the direction as expected. Structured interviews with obese pregnant women identified issues likely to deter women from PA and the importance of how to address the problems of obesity without causing offence, which informed delivery of the intervention. Phase 2, the pilot study, demonstrated the practical feasibility and, importantly, the clinical effectiveness of the intervention to reduce the self-reported dietary GL and saturated fat intake, with a modest increase in PA. Finally, phase 3, the UPBEAT RCT, demonstrated that, despite evidence of improved dietary and PA behaviours, this approach did not lead to a reduction in GDM in obese pregnant women or the number of deliveries of LGA infants.

Although clinical outcomes were not improved by the UPBEAT intervention, ongoing follow-up of the UPBEAT mothers and children will determine whether or not the improvements in maternal diet and PA are maintained, and whether or not the risk of obesity in the children is affected by improved health behaviours in the mother during and after pregnancy.

Recommendations

Research recommendations

- Alternative strategies for reducing the risk of GDM in obese pregnant women and the number of LGA infant deliveries, other than reducing the GL and saturated fat intake in unselected obese women, as described in this programme, should be considered. These include:
  - A major public health focus on development of clinically effective interventions to prevent obesity in women of reproductive age.
  - Development of clinically effective interventions to reduce weight retention following pregnancy, thereby reducing the risk of adverse outcomes, including GDM, in the next pregnancy.
  - Development of risk stratification tools in early pregnancy to enable targeted early pregnancy interventions. These may include diet and PA and/or pharmacological interventions. Delivery of a clinically effective intervention to all obese pregnant women irrespective of risk would incur major health-care costs, as the prevalence of obesity is already high and increasing globally.
- Interventions that successfully change behaviour in obese pregnant women may have benefits through improved dietary behaviours and reduced body fat mass during and beyond pregnancy. Follow-up studies are warranted to determine the longer-term implications for the mother and child.

Clinical recommendations

- The UPBEAT intervention provides an evidence-based strategy to improve maternal diet, reduce maternal body fat and reduce GWG in obese pregnant women.
- As the prevalence of LGA infant deliveries and other neonatal adverse outcomes was lower than expected in obese pregnant women in the UPBEAT intervention, we recommend a RCT to investigate the number of LGA infant deliveries and related maternal and neonatal outcomes following diagnosis of GDM in obese pregnant women by IADPSG's diagnostic criteria with previous World Health Organization and/or current National Institute for Health and Care Excellence diagnostic criteria.
- Current guidelines for screening and treatment of obese pregnant women for GDM should be more widely adopted to reduce associated adverse outcomes.

Trial registration

This trial is registered as ISRCTN89971375 and UK Clinical Research Network Portfolio 5035.

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