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Plenary 1: Building the Science of Nutrition: back to basics? *What we have learned…and where to from here?*

Perinatal nutrition and implications for lifelong health lessons from animal model studies

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There is a U shaped relationship between birth weight and adult fat mass, with a higher prevalence of adult obesity occurring in individuals with birth weights at either the low or high end of the birth weight distribution. Currently more than half of all adults in Australia and the US are either overweight or obese including women of reproductive age and there are now concerns about the emergence of an 'intergenerational cycle of obesity'. For heavy mothers, there appear to be separate contributions of maternal weight before pregnancy and glucose intolerance during pregnancy to birth weight, infant fat mass and the risk of later obesity. It is not clear, however, why the effects of the nutritional environment experienced by the embryo and fetus in utero persist after birth. This presentation will review a series of experimental studies which have investigated how exposure to either maternal overnutrition and/or weight loss at different stages of development, including around the time of conception, can program the metabolic health of the offspring. Experimental studies highlight that there may be separate influences of maternal obesity during the periconceptional period and late gestation on the adiposity of the offspring. Experimental studies have also shown that while a period of dietary restriction in obese mothers in the periconceptional period may ablate the programming of obesity, it is associated with an activation of the stress axis and changes within tissues of metabolic importance including the liver and muscle in the offspring. Thus maternal obesity may result in epigenetic changes which predict the need for efficient fat storage in postnatal life while maternal weight loss may lead to epigenetic changes which predict later adversity. Thus development of dietary interventions for obese mothers during the periconceptional period requires a stronger evidence base which allows the effective weighing up of the metabolic benefits and costs for the offspring.

Plenary 1: Building the Science of Nutrition: back to basics? *What we have learned…and where to from here?*

Perinatal nutrition and implications for life long health: evidence for humans

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Background

The concept that nutrition during the perinatal period can result in permanent health consequences is perhaps best highlighted by the establishment of the folate requirement to minimise the occurrence of neural tube defects in randomised controlled trials. These data highlighted that folic acid supplementation during early pregnancy, covering the period in which the neural tube closes, will result in a 72% reduction in the incidence of neural tube defects such as spina bifida which are associated with significant morbidity and mortality. Although not every nutritional intervention will result in such clear and specific outcomes, there is increasing recognition that improved nutrition during critical periods of development is important to optimise the development of the brain and nervous system and hence the capacity of future generations. Two specific nutrients of interest are iron and the n-3 (or omega-3) long chain polyunsaturated fatty acids (LCPUFA), called docosahexaenoic acid (DHA, 22:6n-3).

Objective

To determine whether additional dietary iron or DHA are necessary to enhance neurodevelopment in early childhood using the randomised controlled trials, AMBIT (Adelaide Mothers' and Babies' Iron Trial), DINO (DHA for the Improvement of Neurodevelopment of preterm infants) and DOMInO (DHA to Optimise Mother Infant Outcome).

Design

In AMBIT, 430 pregnant women were randomly allocated to receive 20mg of iron/day or a placebo tablet from 20 weeks' gestation until birth. The supplement was designed to allow all women to achieve the recommended dietary intake of the time. Neurodevelopment was assessed when children reached 4 years of age.

In DINO, 657 preterm infants born <33 weeks' gestation were randomly allocated to receive a diet with 1% total fatty acids as DHA or a control diet with 0.3% of total fatty acids as DHA. The intervention aimed to deliver the DHA level that a fetus would accumulate during the third trimester of pregnancy and was achieved by supplementing women expressing breast milk for their infants as well as supplementing preterm infant formula to allow for breastfeeding, formula feeding and mixed feeding. Neurodevelopment was assessed at 18 months corrected age.

In DOMInO, 2399 women with singleton pregnancies were randomly allocated to receive either DHA-rich fish oil capsules providing 800mg of DHA/day or vegetable oil

capsules with no DHA from 19 weeks' gestation until birth. Neurodevelopment was assessed when children were 18 months old.

Outcomes

AMBIT: Routine iron supplementation in pregnancy did not alter any aspect of intelligence quotient (IQ) in 4 year old children from women who were not anaemic during mid-pregnancy. Iron supplementation also resulted in more parental reports of abnormal behaviours, an observation which is now consistent with other reports involving iron supplementation of iron replete individuals.
DINO: Supplementation of with high-DHA in the preterm period resulted in a 30% reduction in preterm children with mild cognitive delay and a 50% reduction in preterm children with major cogntive delay at 18 months, although mean scores did not differ between groups. Pre-planned subgroup analyses indicated greater responsiveness of DHA treatment in infants born weighing <1250g and in girls. **DOMInO**: On the other hand supplementing with DHA during the equivalent time in utero did not result in significant improvements in cognitive scores overall or in boys or girls, although fewer children had delayed cognitive development. Similarly the overall language scores did not differ between groups but the language scores of girls were lower with DHA treatment. Important subgroups of preterm infants will benefit from higher-dose DHA supplementation during the preterm period, while DHA supplementation during pregnancy provides little neurodevelopmental benefit to the off-spring in early childhood.

Conclusion

Careful consideration is needed to assess risk-benefit balance and to better target interventions to specific population sub-groups.

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