Proceedings of the Nutrition Society (2021), **80 (OCE5)**, E224 doi:10.1017/S0029665121003529

Summer Conference, 6–8 July 2021, Nutrition in a changing world

Sweet child o' mine – The impact of in utero exposure to the artificial sweetener Acesulfame-k on offspring metabolic outcomes in a mouse model

P.E. Bridge-Comer[1], A.P.M. Spada[1], J. Morton-Jones[1], M.H. Vickers[1] and C.M. Reynolds[1,2]
[1]*Liggins Institute, University of Auckland, Auckland, New Zealand and*
[2]*School of Public Health, Physiotherapy and Sports Science/Conway Institute/Institute of Food and Health, University College Dublin, Belfield, Dublin, Ireland*

Unhealthy diets greatly increase the risk of complications during pregnancy and predisposes offspring to metabolic dysfunction and obesity[1]. While fat intake is typically associated with the onset of obesity and its comorbidities, there is increasing evidence linking sugar to the global rise in obesity rates[2]. Guidelines advising pregnant women to avoid food and beverages with high fat and sugar have led to an increase in consumption of "diet" or "light" options, however, there is limited information regarding the impact of artificially sweetened products during pregnancy on the long-term risk of cardio-metabolic complications in adult offspring. This study aimed to examine the influence of acesulfame-k, a commonly consumed artificial sweetener, on offspring glucose tolerance and adipose tissue biology.

Pregnant female C57BL/6 mice received standard chow ad-libitum with either water (CD), fructose (Fr;20% kcal intake), or AS (AS;12.5 mM Acesulfame-K) throughout pregnancy (n = 8/group). These concentrations represented the equivalent of daily consumption of a 330 ml can of soda or diet soda. These treatments were maintained until pups were weaned (3 weeks postpartum). Pups were housed in same-sex sibling pairs after weaning (n = 8 litters/group) and received a CD diet for the remainder of the experiment. Body weight, food and water intakes were measured weekly. Oral glucose tolerance tests (OGTT) were undertaken at 12 weeks and offspring were culled at week 14. Adipose tissue was dissected and weighed. Samples were collected in 10% neutral buffered formalin for histological analysis or snap frozen in liquid nitrogen for molecular analysis. Adipocyte size was determined following haematoxylin and eosin staining using ImageJ software. Fasn and Foxo1, markers relating to adipogenesis were examined by RT-PCR to determine mechanistic insight into adipogenic potential, in adipose tissue and expressed as fold change relative to control. Data were analysed by one-way ANOVA and repeated measures as appropriate, with Bonferroni post-hoc test. All data are presented as means ± SEM.

There was no significant difference in birthweight between groups. OGTT area under the curve showed that female but not male AS offspring exhibited decreased glucose tolerance compared to the Fr group (1578±110 vs 1264±98; $P < 0.001$) and trended towards a decrease as compared to the CD group (1578±110 vs 1457±120 $P = 0.07$). There was a significant increase in adipocyte size in male offspring from AS (5106±379μm2vs 3423±316μm2; $P = 0.0035$) and Fr (5171±242μm2 vs 3423±316μm2; $P = 0.002$) compared to CD groups in the gonadal fat depot. In female offspring adipocyte size was increased but this only reached significance in the Fr (4204 ±403μm2 vs 2853±202μm2; $P = 0.009$) compared to the CD group. In female but not male offspring there was a significant increase in Fasn gene expression in both AS (0.9±0.01 vs 3.3±0.8; $P = 0.02$) and Fr (0.9±0.01 vs 1.8±0.2; $P = 0.014$) and a decreased FOXO-1 expression in the AS (1.2±0.05 vs 0.9±0.07; $P = 0.02$) and Fr (1.2±0.05 vs 0.8±0.09; $P = 0.01$) compared to the CD group.

In utero exposure to acesulfame-k via the maternal diet increases glucose intolerance and negatively impacts adipocyte size and gene expression in a sex-specific manner. This may have implications in terms of providing tailored dietary advice for pregnant women and highlights the potential negative influence of artificial sweetener composition in an intergenerational context. However, this study has been carried out in a pre-clinical model and further studies in humans would be required to translate these findings to a human setting.

References

1. Reynolds CM, Gray C, Li M, *et al.* (2015) *Nutrients* **7**(9), 8090–111.
2. Johnson RJ, Nakagawa T, Sanchez-Lozada LG, *et al.* (2013) *Diabetes* **62**(10), 3307–15.