Proceedings of the Nutrition Society (2023), **82 (OCE2)**, E176 doi:10.1017/S0029665123001854

46th Annual Scientific Meeting of the Nutrition Society of Australia, 29 November – 2 December 2022, Sustainable nutrition for a healthy life

Oral alanyl-glutamine supplementation improves liver oxidative stress and lipid metabolism in obese and diabetic Ob/Ob mice

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The prevalence of obesity and associated chronic diseases, such as type 2 diabetes mellitus (T2DM) continue to raise worldwide.(1) In the pathophysiology of T2DM induced by obesity, there is a lack of studies investigating the metabolic impairments and supplementation effects of amino acids, such as glutamine.(2) Glutamine is essential for cell homeostasis and function and has antioxidant properties mediated by the glutathione (GSH) system.(3) Here, we aimed to investigate the effects of oral glutamine supplementation on glucose metabolism and antioxidant defence system in obese and diabetic Ob/Ob mice. Ob/Ob (C57BL/6-Lepob) mice ($n = 6$ per group) were orally supplemented with L-alanyl-L-glutamine (DIP), L-glutamine (GLN) or L-alanine for 40 days. Ob/Ob controls (CTRL) and C57BL/6 wild type (WT) animals received fresh water only. During the study, biometric parameters were analysed, such as body weight and food consumption, as well as glucose homeostasis via insulin (ITT) and glucose (GTT) tolerance tests. After euthanasia, blood and tissue samples were collected for lipid profile, oxidative stress markers and histology. Data were analysed using one-way ANOVA followed by Tukey posthoc-test ($p < 0.05$). When compared to Ob/Ob CTRL mice, DIP supplementation increased ($p < 0.05$) glutamine levels in plasma (1.11 mmol/L ± 0.07 vs.1.54 ± 0.10), liver (3.90 µmol/g fresh tissue ± 0.41 v. 5.81 ± 0.41) and skeletal muscle (6.75 µmol/g fresh tissue ± 0.36 v. 9.83 ± 0.36). Free GLN (8.98 ± 0.65) or free ALA (10.50 ± 0.84) only restored skeletal muscle glutamine levels. DIP and GLN supply reduced ($p < 0.05$) basal hyperglycaemia (166 mg/dL ± 8 and 165 ± 110, respectively) and hyperinsulinaemia (5.3 ng/ml ± 0.5 and 5.9 ± 0.5) observed in Ob/Ob CTRL (200 ± 6 and 8.3 ± 0.6). However, only the DIP group showed improvements in GTT and ITT AUC (34169 ± 1888 and 18752 ± 866, respectively) when compared to CTRL (42600 ± 2890 and 22730 ± 1185). Plasma and liver triglycerides, liver fat droplets and plasma cholesterol were approximately 42% lower in all amino acid–supplemented groups, as compared to CTRL. When compared to the CTRL, DIP group shown a reduction ($p < 0.05$) in skeletal muscle (4.71 ± 0.67 v. 2.75 ± 0.46) and liver (4.51 MDA/g fresh tissue ± 0.55 v. 2.45 ± 0.40) TBARS. Moreover, the redox state of the cell, measured by the GSSG/GSH ratio was reduced ($p < 0.05$) in the DIP (0.22 ± 0.02) and GLN (0.21 ± 0.03) groups when compared to the controls (0.53 ± 0.07). Glutamine supplementation in the form of DIP improves body glutamine stores, which has improved glucose homeostasis, liver oxidative stress and lipid metabolism in obese and diabetic Ob/Ob mice.

References

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