Poorly controlled type 1 diabetes is associated with altered glutathione homeostasis in adolescents: apparent resistance to N-acetylcysteine supplementation.

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Abstract

Blood glutathione concentrations represent a measure of protection against oxidative damage. In earlier studies, we observed that, in adolescents with poorly controlled type 1 diabetes mellitus (T1DM), blood glutathione is significantly depleted because of increased rates of glutathione utilization. To determine whether increased availability of cysteine - one of the three constitutive amino acids of glutathione - would attenuate the alterations in glutathione metabolism, ten 16 +/- 1 yr-old adolescents with poorly controlled T1DM [hemoglobin A1c (HbA1c): 9.9 +/- 1.3%] received 5-h infusions of L-[3,3-(2)H(2)] cysteine and d-[6,6-(2)H(2)] glucose on two occasions, 3 wk apart, after a 10-d oral supplementation with (i) N-acetylcysteine (NAC, 30-45 mg/kg/d) or (ii) L-alanine, in randomized order, and with a 3-wk 'washout' interim period. Blood glucose was maintained in the same hyperglycemic range on both infusion study days, using intravenous insulin. Glutathione fractional synthesis rate (FSR) was determined from (2)H(2)-cysteine incorporation into blood glutathione. NAC supplementation failed to raise erythrocyte cysteine concentrations (23 +/- 6 vs. 17 +/- 1 micromol/L, p = 0.853) and did not alter erythrocyte glutathione concentrations (838 +/- 106 vs. 793 +/- 111 micromol/L, p = 0.220) or glutathione FSR (96 +/- 20 vs. 89 +/- 19%/d, p = 0.974). We conclude that in adolescents with poorly controlled T1DM, dietary cysteine supplementation alone cannot correct glutathione status. In the presence of relative insulinopenia, either higher amino acid doses or aggressive insulin therapy may be needed to achieve this goal. This would require further study.

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