Proceedings of the Nutrition Society (2008), **67 (OCE8)**, E424 doi:10.1017/S0029665108000980

Summer Meeting 30 June–3 July 2008

Possible histaminergic modulation of energy expenditure and blood glucose regulation in man

Varsha Rajashekar[1], Frank Hucklebridge[1], Orla Kennedy[2] and Adam Cunliffe[1]
[1]*University of Westminster, London, UK and* [2]*University of Reading, Reading, UK*

Syndrome X or metabolic syndrome is a cluster of metabolic abnormalities, which comprise obesity, insulin resistance, hyperlipidaemia and high blood pressure, and is associated with increased risk of CVD and thus increased mortality rates[(1)]. Risk factors for this disorder include unhealthy eating and lack of physical activity along with modest weight gain. This syndrome is fortunately reversible and modest weight loss leads to improvement of the other components of the syndrome[(2)].

Along with conservative modes of treatment such as hypoenergetic diets, increased physical activity and moderation of salt and saturated fat intake, research is needed to elicit the suitability of natural micronutrients that affect energy expenditure and blood sugar regulation. One such micronutrient is the essential amino acid L-histidine. L-Histidine occurs naturally in fermented foods, meat and fish. It is also sold as a supplement and there are no known toxic effects of this amino acid. Previous studies have shown that modulation of hypothalamic histamine by H3 receptors, possibly by signalling through H1 receptors leads to alterations in feeding behaviour in animals and may result in body-weight changes[(3,4)].

The present study has examined the effects of 10 d of supplementation with L-histidine (25 mg/kg per d) on energy expenditure, mean skin and core temperature and fasting blood glucose of nine healthy male subjects (age 24.8 (SD 6.1) years, BMI 23.8 (SD 1.8) kg/m^2, body weight 75.4 (SD 3.9) kg and fasting blood sugar 5.4 (SD 0.8) mmol/l), using a single-blinded cross-over (with a wash-out period) randomised placebo-controlled (Casilan-90 (Complan Foods Ltd, Egham, Surrey, UK); 45 mg/kg per d) design. Oral administration of L-histidine reduced mean body weight by 1.4% ($P=0.009$) and mean fasting blood glucose by 11% ($P=0.04$), in comparison with the placebo.

	Baseline		Post placebo intake		Post L-histidine intake	
	Mean	SD	Mean	SD	Mean	SD
% Body fat	16.0	3.2	15.6	3.4	15.5	3.1
BMR (kJ/d)	6977	563	7344	772	7378	1156
FBS (mmol/l)	5.4	0.8	4.9	0.5	4.8*	0.5

n 9. FBS, fasting blood sugar. Value was significantly different from baseline measurement (ANOVA): *$P=0.04$.

These data demonstrate that oral supplementation of L-histidine improves biochemical indices of blood glucose regulation and reduces body weight. The mechanisms by which L-histidine exerts these effects are not clearly established, but may involve activation of histamine neurons leading to sympathetic augmentation of lipolytic activity and chelating action of L-histidine on Zn, which stimulates intestinal absorption of Zn, in turn regulating insulin receptor-initiated signal transduction mechanisms and insulin receptor synthesis, both of which require further investigation.

1. Day C (2007) *Diab Vasc Dis Res* **4**, 32–38.
2. Stone NJ & Saxon D (2005) *Am J Cardiol* **96**, 15E–21E.
3. Masaki T, Yoshimatsu H, Chiba S, Watanabe T & Sakata T (2001) *Diabetes* **50**, 376–384.
4. Takahashi K, Suwa H, Ishikawa T & Kotani H (2002) *J Clin Invest* **110**, 1791–1799.