The Role of Intestinal Diamine Oxidase Deficiency in Urticaria

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The enzyme diamine oxidase (DAO) is almost exclusively confined to the intestinal mucosa where it plays important roles in the metabolism of the poly-amines and the degradation of histamine (histami-nase). Unstimulated plasma DAO is close to assay detection limits but the enzyme can be released into the circulation by low-dose (5,000 U) i.v. heparin. The resultant area under the plasma concentration-time curve (AUC: measured every 15 min for 2 h) correlates linearly with intestinal mucosal DAO activity (Rokkas et al, Gut 1986;27:A630) suggesting that the AUC provides a noninvasive marker of intestinal DAO activity. Patients with chronic idiopathic urticaria (+ intestinal mucosal oedema and colic) are intolerant of exogenous i.v. histamine and degrade it more slowly than controls [Murdoch et al, Clin Exp Allergy 1989; 19:103]. Histamine is catabolised mainly by histaminase + prior hepatic methylation. We postulated, therefore, that the slow degradation of infused histamine in urticaria patients might be due to a deficiency of intestinal mucosal DAO. To test this hypothesis, we measured post-heparin plasma DAO profiles in 17 controls and 14 patients with chronic (> 3 months) recurrent (> 5 attacks) urticaria. The mean AUC in the patients (16.9 ± 13.3 mU·l⁻¹·h⁻¹) was significantly (p < 0.002) less than that in the controls (35.8 ± 20.8). Despite the scatter of results, six of the 14 patients had little or no rise in plasma DAO after the i.v. heparin and no overlap in AUCs with the controls. To confirm that the low AUCs in these patients did indeed reflect intestinal mucosal DAO deficiency, 6 of the 14 consented to peroral jejunal biopsies. Four had virtually no mucosal DAO activity (0.7-1.2 mU/g mucosal protein) compared with that in controls (22.4 ± 16.4) but in the remaining two, DAO levels (16 and 53 mU/g) were in the normal range. Moreover, when the results in the urticaria patients were added to our previous control data [Rokkas et al, 1986], the significance of the linear regression correlating post-heparin plasma and jejunal mucosal DAO activity was maintained (r=0.84; p < 0.01).

Conclusion: In some, but not all, patients with chronic urticaria ± recurrent abdominal colic, the associated defect in histamine degradation seems to be due to intestinal mucosal DAO deficiency. Thus patients with urticaria may have a newly-recognised, primary intestinal disease.