ACUTE INTESTINAL INJURY IS EXACERBATED BY VITAMIN A DEFICIENCY

R.A. WARDEN, R.S. NOLTORP, J.L. FRANCIS, P.R. DUNKLEY and E.V. O'LOUGHLIN

Supplementation with vitamin A has been shown to significantly reduce diarrhoeal disease mortality in developing countries (where both diarrhoeal disease and vitamin A deficiency are prevalent) (Glasziou and Mackerras 1993). Symptoms of diarrhoeal disease occur due to damage to intestinal structure and function. We postulated that vitamin A deficiency may exacerbate intestinal damage caused by an acute injury.

Methods: Three groups of weanling male SPF Wistar rats were fed for 40-42 days: (1) vitamin A deficient diet (VA^-); (2) vitamin A deficient diet, pair fed to animals in group 1, vitamin A (125 IU/day) added to drinking water (PF); (3) ad libitum vitamin A deficient diet, vitamin A (125 IU/day) added to drinking water (AD LIB). Methotrexate (MTX) was used to induce an acute intestinal injury. MTX (7 mg/kg ip) or vehicle was administered five days prior to sacrifice for three consecutive days. Clinical features of diarrhoeal disease (diarrhoea, weight loss) were monitored, and serum retinol assessed at sacrifice. Light microscopy was performed on jejunal segments and jejunal mucosal wet weight, protein and sucrase activity were measured.

Results: Significantly more VA^- MTX rats developed diarrhoea than PFMTX or AD LIB MTX rats ($P<0.02$), and more dramatic weight loss occurred in the VA^- MTX animals than in the PFMTX or AD LIB MTX animals ($P<0.001$). Serum retinol was negligible in VA^- rats. Gross destruction of villous architecture was observed in VA^- MTX rats, while partial villous atrophy occurred in PFMTX animals. MTX significantly reduced jejunal mucosal parameters measured in both VA^- and PF animals ($P<0.05$). Data for PFMTX and VA^- MTX animals are presented below as mean ± SE.

	PFMTX (n=20)	VA^- MTX (n=17)
Mucosal wet weight (mg/cm)	27.0 ± 1.8	20.0 ± 2.5
Protein (g/cm)	2.3 ± 0.2	1.9 ± 0.3
Sucrase (U/g protein)	36.5 ± 8.9	6.5 ± 2.9[a]

[a]$P<0.05$ compared to PFMTX

Conclusions: Vitamin A deficiency exacerbates MTX induced intestinal injury, causing an increase in the incidence of diarrhoea, severity of weight loss and reduction in sucrase activity. These findings may provide an explanation for the epidemiological findings linking vitamin A deficiency with increased mortality due to diarrhoeal diseases.

GLASZIOU, P.P. and MACKERRAS, D.E.M. (1993). Lancet 306: 366.

Disciplines of Medical Biochemistry and Paediatrics, University of Newcastle, New South Wales 2308