Intestinal permeability in vitamin A deficient rats

RA Warden[1], RS Noltorp[2], CJ Bell[3], PR Dunkley[1], EV O'Loughlin[2]

[1]Faculty of Medicine and Health Sciences, University of Newcastle, NSW 2308
[2]Department of Paediatrics, John Hunter Hospital, NSW 2310
[3]Department of Gastroenterology, Royal North Shore Hospital, NSW 2065

There is strong epidemiological evidence for a relationship between diarrhoeal disease and vitamin A deficiency in children in areas (particularly in developing countries) where diarrhoeal diseases are responsible for significant childhood morbidity and mortality (1). Changes in intestinal permeability may be the mechanism responsible for this association. We have previously found villous atrophy and reduced disaccharidase activity in clinically vitamin A deficient rats (2). Our aim in the present study was to investigate the effect of sub-clinical vitamin A deficiency on rat intestinal permeability.

Vitamin A deficiency was induced by feeding weanling male wistar rats a vitamin A deficient diet (VA-) for either six weeks (sub-clinical deficiency) or nine weeks (clinical deficiency). For each time period, there were also two control groups: PF (pair fed to VA-, 75 μg vitamin A/day added to drinking water. Intestinal permeability was measured in vivo in anaesthetised rats using ^{51}Cr-EDTA, instilled into a ligated jejunal loop, with carotid blood sampled 30 and 60 mins later.

In the 40-42 day study, intestinal permeability was significantly greater in VA- rats than the PF rats at both time periods ($P<0.04$). However, in the longer study, there was no difference between these groups, although there was a trend for VA- rats to have greater permeability than VA+ rats. ^{51}Cr-EDTA permeability at 30 mins is shown in the table below.

	30 min ^{51}Cr-EDTA permeability[1] (% instilled label/ml plasma/g loop wet weight x 10^{-2})		
	VA- (n≥7)	PF (n≥7)	VA+ (n≥7)
6 weeks	2.40 ± 0.22	1.45 ± 0.28*	2.89 ± 0.60
9 weeks	3.20 ± 0.75	4.16 ± 1.62	1.38 ± 0.44

[1]mean ± sem; *P = 0.014 vs VA-

Intestinal permeability was greater than that of equally (mal)nourished rats in early vitamin A deficiency. However, as vitamin A deficiency becomes more severe, this effect appears to be subsumed by that of malnutrition per se. An inability to reduce intestinal permeability (and hence enhance intestinal barrier fucntion) may provide a mechanistic explanation for the increased mortality from diarrhoeal disease in subclinical vitamin A deficiency.

1. Glasziou PP, Mackerras DEM. Vitamin A supplementation in infectious diseases: a meta-analysis. Lancet 1993;306:366-70.
2. Warden RA, Strazzari MJ, Dunkley PR, O'Loughlin EV. Vitamin A deficient rats have only mild changes to jejunal structure and function. J Nutr 1996;126:1817-26.