

Absorption of vitamin A by children with diarrhoea during treatment with oral rehydration salt solution*

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The results of a study of absorption by children of vitamin A indicate that absorption is lower in children with acute diarrhoea compared with normal children. The glucose or electrolytes present in solutions of oral rehydration salts had no effect on the absorption. Despite malabsorption, 70% of the administered dose of 100 000 IU of vitamin A in 500 ml of fluid was absorbed and retained.

Vitamin A deficiency is a significant health problem in many developing countries. In India the results of several surveys indicate that 5-10% of children present ocular signs of vitamin A deficiency (1). Inadequate dietary intake of vitamin A is the major cause of xerophthalmia. Furthermore, other factors that influence vitamin A metabolism, such as protein-energy malnutrition and infection, contribute to the disease process. Keratomalacia is often preceded by an episode of infection, and diarrhoea is an important risk factor for this condition (2). Oral rehydration therapy is now widely used at the community level for the control of diarrhoeal morbidity. Incorporation of vitamin A into oral rehydration salt (ORS) solutions has been proposed as a public health measure to reduce the risk of xerophthalmia following diarrhoea; however, there is some evidence that the absorption of vitamin A is altered during episodes of diarrhoea (3, 4). The present study was therefore undertaken to determine the extent to which vitamin A supplements given as part of oral rehydration therapy are absorbed by children with diarrhoea.

MATERIALS AND METHODS

Nineteen children with diarrhoea, passing 5-10

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loose stools per day, formed the basis of the study and were investigated in a metabolic ward. At the time of admission all had mild to moderate dehydration. Sixteen control children without diarrhoea were also included in the study. Only boys were selected since accurate collection of stools and urine is difficult from girls. Both sets of children belonged to low socioeconomic groups, and their ages ranged from 1 to 4 years. Mean ages and weights are shown in Table 1. None of the children exhibited clinical signs of malnutrition.

Absorption of vitamin A by the children was determined using tritium-labelled vitamin A. The study was reviewed and ethical approval obtained before being carried out. Consent of the children's parents was also obtained prior to commencement. Each child was administered a dose of 2 μ Ci retinyl-11,12-³H₂ acetate (specific activity, 380 μ Ci/mg) incorporated into 100 000 IU of water-miscible vitamin A. Half the children in each group received the dose along with 500 ml of ORS solution, while the other half received the dose with 500 ml of water. The composition of ORS solution used was that recommended by WHO (sodium chloride, 3.5 g; sodium bicarbonate, 2.5 g; potassium chloride, 1.5 g; and glucose 20 g in 1 litre water).

The labelled vitamin A in the ORS solution or water was administered to the children over 4-6 hours. For 4 consecutive days after the dose was given, 24-hour samples of faeces and urine were collected from each child. Radioactivity in the samples was measured using a liquid scintillation counter^a with a counting efficiency of 33% for tritium. Quench corrections were made using appropriate internal standards.

^a Packard Tri-carb liquid scintillation spectrometer (model 3255).

Table 1. Characteristics of the children in the study

Treatment	Mean age (months)	Mean weight (kg)	No. with grade I malnutrition ^a	No. with grade II malnutrition ^a
<i>Children with diarrhoea</i>				
Vitamin A + ORS	11.8 ± 1.6	6.92 ± 0.40	2	8
Vitamin A + water	10.1 ± 0.8	7.10 ± 0.34	5	4
<i>Children without diarrhoea</i>				
Vitamin A + ORS	17.3 ± 4.1	7.9 ± 0.1	2	6
Vitamin A + water	28.8 ± 3.0	10.8 ± 0.3	5	3

^a Harvard standards.

Table 2. Data on the absorption of vitamin A by children in the study

Treatment	No. of children	Mean vitamin A absorbed (%)	Mean absorbed vitamin A	
			Excreted in urine (%)	Retained in body (%)
<i>Children with diarrhoea</i>				
Vitamin A + ORS	10	72.2 ± 4.7 ^a	7.0 ± 1.1	67.1 ± 4.4 ^a
Vitamin A + water	9	76.9 ± 3.7 ^a	4.5 ± 0.9	73.1 ± 5.2 ^a
<i>Children without diarrhoea</i>				
Vitamin A + ORS	8	94.3 ± 1.4	8.3 ± 0.5	86.5 ± 1.4
Vitamin A + water	8	93.8 ± 0.7	5.8 ± 0.9	88.3 ± 1.3

^a $P < 0.001$ relative to children without diarrhoea by paired Student's *t*-test.

The total radioactivity in the urine samples and in ethanol extracts of the faeces was determined using a dioxane-based scintillation mixture (5). Samples of urine and faeces were also saponified and extracted with hexane. The hexane extracts were taken up in toluene, and the radioactivity in the unsaponifiable fraction was measured. The difference in radioactivity of the total and unsaponifiable fractions was taken to be equal to that of the water-soluble fraction.

Blood samples were collected from 27 of the 35 children studied, both at the beginning of the study and again 24 hours after the dose of vitamin A had been administered. The level of vitamin A in serum was determined by high performance liquid chromatography (HPLC) using a reversed phase column^b and water-methanol (ratio 5:95) eluant (6).

The stability of vitamin A in ORS solution stored in closed glass containers at room temperature in diffuse sunlight for 24–48 hours was determined. The concentration of vitamin A in 10 samples of ORS solution after 0, 24, and 48 hours was also measured.

^b Altex, Ultrasphere-ODS.

RESULTS

Mixed solutions of vitamin A and ORS were stable at room temperature, and the original amount of vitamin A added to the solution was fully recovered, to within 1% variation, after 48 hours' storage.

After administration of labelled vitamin A to the control children, very little tritium was detected in their faeces. The level of absorption of vitamin A was high, irrespective of whether it was given in solutions of ORS or in water: the mean absorption level was 94.3% and 93.8%, respectively (Table 2). In contrast, for children with diarrhoea, the amount of radiolabel excreted was significantly higher: here, the mean level of vitamin A absorption was 72.2% for ORS solution and 76.9% for water.

Approximately 40% of the radiolabel was detected in the unsaponifiable fraction of faeces, suggesting that vitamin A was excreted unchanged to some extent, while the residual 60% was excreted as water-soluble degradation products. These proportions were the same for the children with diarrhoea and for the controls. About 8% of the radiolabel absorbed

Table 3. Mean levels of vitamin A in the serum of children in the study

Group	No. of children	Mean vitamin A level ($\mu\text{mol/l}$)	
		Basal	After 24 hours
Children without diarrhoea	14	0.63 \pm 0.07	1.1 \pm 0.1 ^a
Children with diarrhoea	13	0.61 \pm 0.1	0.86 \pm 0.13 ^{a, b}

^a $P < 0.001$ relative to basal values by paired Student's *t*-test with log transformations.

^b $P < 0.01$ relative to children without diarrhoea by Student's *t*-test with log transformations.

from the gut was excreted in the urine. All the radioactivity was found in the water-soluble phase, indicating that only vitamin A metabolites are excreted in urine. In this respect there was no difference between children with diarrhoea and the controls.

The amount of vitamin A retained was calculated from the difference between the amount of radiolabelled vitamin A administered and the amount excreted in urine and faeces over a period of 4 days. The controls retained more than 80% of the dose, while for children with diarrhoea the level of retention was significantly lower. There were no differences in this respect for vitamin A administered in ORS solution or in water, either for controls or children with diarrhoea.

Initial levels of serum vitamin A were similar in the study group and controls. However, 24 hours after administration of vitamin A a significant increase in its serum concentration was found, levels being significantly higher in the controls (Table 3). Since there was no difference in this respect between children who had received vitamin A in ORS solution or water, data for these groups were pooled.

DISCUSSION

Very little radioactivity was detected in the faeces of controls who had been administered labelled retinyl acetate along with 100 000 IU of vitamin A, indicating that absorption of the vitamin was almost complete. Previously we reported that absorption of vitamin A depends on the dose administered. At physiological levels the absorption was more than 90%, but with a single massive dose of 200 000 IU of oily vitamin A the mean level of absorption was only 66% (7). Absorption of vitamin A also depends on the type of preparation administered, the absorption being higher for the water-miscible than the oil-

soluble vitamin (8). In the present study, a water-miscible preparation was used and this accounts for the higher absorption efficiency. There was no difference in absorption between vitamin A administered in ORS solution or in water, indicating that the presence of glucose and electrolytes had no influence in this respect.

The amount of radiolabel excreted in the faeces of children with diarrhoea was significantly higher than that of controls. This is consistent with previous observations and indicates that absorption of vitamin A is impaired among children with diarrhoea (3). Nalin & Russell also reported that vitamin A absorption is lower among cases of acute diarrhoea (4). However, the net absorption of vitamin A depends on the amount administered. Previously we reported that approximately 70% (2000 IU) of a physiological dose of 3000 IU vitamin A was absorbed by children with diarrhoea (3). In the present study, children with diarrhoea also exhibited malabsorption; however, since the dose of vitamin A given was large, the net amount absorbed was greater (75 000 IU), and this was reflected in the increased levels of vitamin A in serum after 24 hours. A study in Bangladesh has also shown that substantial amounts of vitamin A are absorbed during bouts of acute diarrhoea if large doses are given (9). Within 4 hours of receiving an oral dose of 7500 IU/kg of water-miscible vitamin A, children exhibited a significant increase in serum concentrations of vitamin A, retinol-binding protein, and provitamin A.

Malnourished children with xerophthalmia often also have diarrhoea. Absorption of vitamin A in these children is impaired but this does not mean that they do not benefit from therapeutic doses of the vitamin. In Indonesia, a study of malnourished children with diarrhoea who were administered an oral dose of 200 000 IU of vitamin A indicated that there was a rapid improvement in corneal xerophthalmia (10): oral administration was found to be as effective as intramuscular injection in this respect. Similar studies have been made of Indian children (1).

Approximately 500 000 cases of corneal xerophthalmia, half of which lead to blindness, occur every year in south-east Asia (11), and several intervention programmes have been initiated for its control on the global scale (12). These include periodic distribution of vitamin A to preschool-age children at risk, nutrition education to increase the intake of vitamin A through local sources, and fortification of staple foods with vitamin A. Since malnourished children with diarrhoea are at greater risk of developing xerophthalmia (2), they need special attention. Oral rehydration therapy is now widely used for the management of diarrhoea, and it has been suggested that vitamin A could be administered along with rehydration fluid. Nalin & Russell have raised doubts

about the efficacy of this approach because absorption of vitamin A is lower during bouts of diarrhoea (3). However, the results of the present study, as well as those of other investigations, indicate that substantial amounts of vitamin A can be absorbed by children with diarrhoea, despite altered intestinal function.

Supplementary vitamin A could be added to the ORS mixture or supplied separately. It must, however, be pointed out that a child may suffer more than one episode of diarrhoea per annum and that repeated administration of large amounts of vitamin A may produce toxic reactions.

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RÉSUMÉ

ABSORPTION DE LA VITAMINE A PAR DES ENFANTS DIARRHÉIQUES AU COURS DU TRAITEMENT PAR LA SOLUTION DE SELS POUR RÉHYDRATATION ORALE

La xérophtalmie pose un problème sanitaire notable dans de nombreux pays en développement et constitue une cause importante de cécité chez les enfants. Cette maladie est souvent associée à l'infection et la diarrhée représente un important facteur déclenchant. La présente étude a été entreprise en vue de déterminer dans quelle mesure la vitamine A administrée avec la solution de sels pour réhydratation orale (SRO) est absorbée par un enfant diarrhéique.

Dix-neuf enfants âgés de 1 à 4 ans, atteints de diarrhée modérée, et 16 témoins d'âge apparié indemnes de diarrhée

ont fait l'objet de cette étude, dans laquelle l'absorption de la vitamine A a été examinée au moyen de vitamine A radio-marquée. Les résultats indiquent que l'absorption de vitamine A était réduite chez les diarrhéiques et que le glucose ou les électrolytes présents dans la solution de SRO n'avaient pas d'effet sur l'absorption. Néanmoins, une proportion notable de la dose de vitamine A administrée a été absorbée et retenue dans l'organisme. Ainsi, quand un enfant diarrhéique recevait 100 000 UI de vitamine A dans 500 ml de liquide, 70% de la dose étaient absorbés et retenus en dépit de la malabsorption.

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