

A RANDOMIZED CONTROLLED TRIAL OF VITAMIN A SUPPLEMENTATION IN ACUTE DIARRHEA

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ABSTRACT

Effect of vitamin A supplementation on duration of diarrhea was evaluated in 108 cases between 6 months to 5 years of age suffering from acute diarrhea of less than 3 days duration and results were compared with equal number of age and sex matched controls having comparable feeding pattern, nutritional and socioeconomic status and clinical profile who did not receive vitamin A supplementation.

There was no significant difference in the mean duration of diarrhea in cases who received vitamin A and the controls. However, on subgroup analysis of the study and control groups a significant ($p=0.009$) beneficial effect of vitamin A supplementation was noticed in cases who had a pre-existing vitamin A deficiency with CIC stage 3/5 and above. Even though vitamin A supplementation in malnourished children did not significantly alter the duration of diarrhea, a beneficial effect was observed in children who had CIC state 3 and above in association with malnutrition ($p=0.025$).

Our results indicate that vitamin A supplementation does not significantly reduce the duration of a diarrheal episode. However, in children with pre-existing vitamin A deficiency particularly those who have associated malnutrition it may have a beneficial effect.

Key words: Acute diarrhea, Vitamin A.

Diarrheal diseases and vitamin A deficiency are common health problems in developing countries. Diarrheal episodes increase vitamin A requirement and lower vitamin A status of the patient(1). One of the important reasons for prolonged duration of diarrhea is believed to be a delay in the repair of the intestinal mucosa. Role of vitamin A in maintaining the integrity of the epithelial cell lining of gastrointestinal tract is well known besides its influence on the immunological status. Hence supplementation of vitamin A early in the course of acute diarrheal illness may reduce the total duration of diarrhea by reducing the intestinal mucosal injury and enhancing the repair of the intestinal cells particularly following invasive diarrhea. This prospective study was planned to evaluate the effect of vitamin A supplementation on duration of acute diarrhea with particular reference to its role in the presence of vitamin A deficiency, severe malnutrition and poor socioeconomic status.

Material and Methods

This randomized controlled trial was conducted in Diarrhea Training and Treatment Unit (DTU) in Kalawati Saran Children's Hospital, New Delhi from September 1992 to June 1993. Children of either sex between 6 months to 5 years of age with a diarrheal duration <72 hours,

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with no vitamin A supplementation given in last 3 months and no history of measles in the preceding 6 weeks were enrolled in the study and were managed according to standard treatment protocol(2). Besides a detailed history and thorough examination, patients were screened for signs of vitamin A deficiency and any systemic illness. Assessment of nutritional status was done according to classification suggested by Nutrition Subcommittee of Indian Academy of Pediatrics(3) and the socioeconomic status by Kuppaswamy scale(4). Conjunctival impression cytology (CIC) was used to detect subclinical vitamin A deficiency(5). Staging of conjunctival morphology was done as per the recommended criteria(6).

Children were randomly assigned to study group (n=108) and control group (n=108) by simple random sampling. All the characteristics of cases and controls (age and sex distribution; feeding pattern; socioeconomic status; nutritional status; clinical profile at the time of enrolment like stool frequency, state of hydration, and associated symptoms like vomiting, fever and bloody stools) were comparable. The study group was administered 1,00,000 IU of vitamin A orally in infants and children less than 10 Kg body weight and 2,00,000 IU to children >1 year and/or body weight >10 Kg. Patients assigned to control group did not receive vitamin A on admission but the ones with clinical as well as subclinical evidence of vitamin A deficiency were given vitamin A after the termination of diarrheal episode. Cases and controls were monitored for frequency of stools/day and duration of diarrhea till the diarrheal episode terminated. Termination of diarrheal episode was defined as passage of stool of normal consistency and a frequency of less than 3/day, for at least 72 hours from the last loose stool. The outcome variables were

compared and statistical analysis done by Chi square test, correlation co-efficient, unpaired 't' test and Wilcoxin rank method wherever applicable.

Results

The study included 108 cases (mean age 11.59 ± 6.93 months) and equal number of controls (mean age 12.06 ± 8.12 months). Xerophthalmia was noticed in 12/108 cases (11.1%) and 14/108 controls (12.9%). Conjunctival impression cytology was possible in 96 cases and 95 controls. Abnormal CIC was detected in 46/94 patients (47.9%) and 47/95 controls (49.5%) including patients of xerophthalmia. Diarrheal episodes in all the cases as well as controls terminated within 10 days and none of them developed persistent diarrhea. The study group had a mean duration of diarrhea of 100.74 ± 43 hours in comparison to control group with 110.49 ± 49.08 hours ($p=0.11$). A statistically significant difference was noticed in the mean duration of diarrheal episodes between various socioeconomic classes ($p=0.006$), but no significant difference was noticed with vitamin A supplementation in each socioeconomic class ($p=0.33$). No significant difference was noticed with regard to nutritional status ($p=0.31$), hydration ($p=0.13$) or etiological organisms ($p=0.59$). However, a significant difference ($p=0.009$) was noticed in the duration of diarrhea between cases and controls having vitamin A deficiency with conjunctival impression cytology stage 3/5 and above (Table I). Eventhough protein energy malnutrition *per se* did not have a significant difference in mean duration of diarrhea between the two groups, a significant difference was noticed in children with malnutrition and CIC stage 3/5 and above ($p=0.025$). No untoward effects of vitamin A supplementation were noticed in any of the cases.

TABLE I-Correlation of Duration of Diarrheal Episodes with Variables

Variables	Cases (n=108)		Controls (n=108)		P value
	Mean	SD	Mean	SD	
<i>Nutritional status</i>					
Normal	78.71	19.94	100.66	59.66	
Mild malnutrition	96.70	43.55	105.52	44.89	0.31
Moderate malnutrition	110.63	44.31	115.34	33.43	
<i>Hydration status</i>					
No dehydration	93.33	30.61	102.31	44.21	
Some dehydration	99.50	43.21	118.91	36.41	0.13
Severe dehydration	103.89	45.28	139.0	50.61	
<i>Conjunctival impression cytology</i>					
Stages 0 & 1	102.54	42.38	111.84	38.92	0.28
Stage 2	102.54	50.78	103.0	38.87	0.70
Stage 3 & above	95.89	19.79	128.46	40.85	0.009
<i>CIC and Nutritional status</i>					
Normal nutrition status with CIC >3/5	91.00	16.46	122.0	68.45	0.51
Malnutrition with CIC >3/5	98.33	22.34	131.33	26.76	0.025
<i>Stool characteristics</i>					
Dysentery	86.16	72.29	75.2	47.09	0.12
Watery	101.74	40.96	112.55	38.98	0.65
<i>Etiological agents</i>					
Escherichia coli Non pathogenic organisms	99.23	23.46	106.00	42.11	0.59
No growth	72.42	41.23	82.51	46.17	
Overall	100.74	43.00	110.49	49.08	0.11

Discussion

The present study was conducted with the hypothesis that vitamin A supplementation can reduce the duration of diarrhea by virtue of its role in epithelial cell integrity and as an immune modulant. This belief is

supported by the fact that a longer duration of diarrhea has been reported in subjects with vitamin A deficiency(7). In another study(8), a significant reduction in the incidence of diarrhea has been observed following administration of large dose vitamin A supplementation. However, our results

indicate that vitamin A supplementation early in the course of diarrheal episode did not significantly alter the mean duration of diarrhea. On subgroup analysis of cases and controls, a beneficial effect of vitamin A supplementation was observed to be limited only to those cases who had a pre-existing vitamin A deficiency (clinical as well as subclinical) and in those children having vitamin A deficiency with associated malnutrition.

Malnutrition tends to prolong the duration of diarrheal episodes(7,9,10) presumably due to delayed mucosal recovery after initial insult. By virtue of its effect on intestinal epithelial cell integrity and immune modulation, vitamin A supplementation is expected to have a beneficial effect. Our results do not support this view since no significant difference was noticed in cases and control in various grades of malnutrition. However, diarrheal episodes in malnourished children associated with vitamin A deficiency may be benefited by vitamin A supplementation.

Poor socioeconomic status may not be directly responsible for prolonging the duration of a diarrheal episode. However, other factors like malnutrition and poor environmental sanitation, which are closely related to socioeconomic status have been incriminated in the etiology of persistent diarrhea(7,9,11). A significant difference was noticed in the duration of diarrheal episodes in children from poorer socioeconomic strata (class 3 and 4) in both cases and controls ($p=0.006$). However, supplementation of vitamin A did not have any beneficial effect in reducing the duration of diarrhea in any of the socioeconomic classes.

Clinical variables like state of hydration at the time of admission may suggest the

type of mucosal injury and underlying etiological agent. Our results indicate a higher mean duration of diarrhea in patients with severe dehydration in cases as well as controls but statistically insignificant. Supplementation of vitamin A did not significantly reduce the duration of diarrhea with severe dehydration ($p=0.13$). Duration of diarrhea is also reported to be prolonged in patients who present with bloody diarrhea(7,11) presumably due to severe mucosal damage and longer time required for recovery. Our results are in contrast to this view since mean duration of diarrhea in both cases and controls with dysentery was shorter in comparison to those with watery diarrhea. Vitamin A supplementation may enhance the recovery of intestinal mucosa in dysentery. However, no beneficial effect of vitamin A supplementation was noted in our patients with bloody diarrhea. The discrepancy between the results of other workers(7,11) and our findings could be because of small number of cases and controls in the dysentery group.

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