
Original Articles

EFFECT OF ADMINISTRATION OF 200,000 IU OF VITAMIN A TO WOMEN WITHIN 24 HRS AFTER DELIVERY ON RESPONSE TO OPV ADMINISTERED TO THE NEWBORN**P. Bhaskaram and N. Balakrishna**

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Objective: To explore the effect of maternal supplementation of vitamin A on the immune response to oral polio vaccine in breastfed infants **Design:** Randomized controlled trial **Setting:** Hospital based **Methods:** One hundred mothers having uncomplicated deliveries randomly received either 200,000 IU vitamin A orally (Experimental) or placebo (Control) All the newborns were given a dose of oral polio vaccine within 72 hours after birth and were breastfed Type specific neutralizing antibodies to polio viruses in test sera diluted from 1:4 to 1:512 and serum retinol levels were determined from the cord blood and at the age of 6 weeks Breast milk retinol levels were determined at 3, 10, 30, 45 and 90 days of lactation **Results:** Seroconversion to OPV and geometric means of antibody titers to the three types of polio viruses were comparable between the groups of infants belonging to the experimental and control mothers Breast milk retinol levels were significantly higher in the experimental group upto 45-90 days of lactation. Majority of the infants at birth had serum retinol levels <15 µg/dl which improved significantly by 6 weeks irrespective of the maternal supplementation status **Conclusions:** Maternal vitamin A supplementation soon after delivery improves vitamin A intakes of breastfed infants during the first 3 months and has no interference with the seroconversion to a neonatal dose of OPV OPV administered to newborn in turn has no adverse effect on the vitamin A status of the breastfed infants.

Key words: Oral Polio Vaccine, Vitamin A.

VITAMIN A deficiency is one of the nutritional problems of public health magnitude due to its adverse effects on vision among preschool children in developing countries Besides this, recent research has identified the effects of even mild vitamin A deficiency in aggravating morbidity due to infections in young chil-

Dren(1). Sommer *et al.* convincingly demonstrated significant reversal of these effects with improvement in child survival following vitamin A administration(2). These observations led to the recommendation of administration of large dose supplementation of vitamin A to infants above 6 months of age in countries endemic for vitamin A

deficiency. Supplementation of lactating mothers has been proposed as an alternate strategy to increase vitamin A intake of breastfed infants younger than 6 months of age(3). Administration of vitamin A has been linked with the ongoing primary immunization programmes to achieve maximum cost effectiveness and to improve coverage(4). However, the effects of such a combined schedule on response to live viral vaccines has been intensely debated(5,6).

In a recent study we found mutually beneficial effects when the combined schedule of measles vaccination and 100,000 IU vitamin A supplementation was administered to 9 months old infants(7). In the present investigation we explored the interactions of 200,000 IU of vitamin A administered to mothers soon after delivery and oral polio vaccine (OPV) administered in the newborn period of breastfed infants.

Subjects and Methods

One hundred infants born at the end of a healthy term pregnancy were registered for the study along with their mothers. All the infants received a dose of OPV between 48 and 72 hours after birth. The mothers were randomly allocated into two groups, the experimental group receiving 200,000 IU of vitamin A as a single oral dose within 24 hours after delivery, and the control group receiving a placebo. Cord blood samples and venous blood samples of all the infants at 6 weeks of age were collected for assay of type specific polio viral antibodies and serum retinol. Polio antibodies were determined according to the classical microneutralization test earlier followed by us in sera diluted from 1:4 to 1:512(8). Titres of 1:4 and above were scored as positive for antibodies against the respective strains of the virus tested. A pooled serum

sample was included as an internal standard with each assay system. Seroconversion rates were calculated as four fold or greater rise in antibody titers over the level at birth taking into consideration that the transplacentally acquired maternal antibodies have a half-life of about 3-4 weeks(9). Serum vitamin A was assayed using the fluorometric method(10). Breast milk samples from all the members were collected on days 3, 10, 30, 45 and 90 of lactation for determination of retinol levels using colorimetric method(11). Breast milk was collected in all the mothers by complete emptying of left breast at 8 a.m. All the infants were breast fed during the study period. They were closely monitored from birth to 5 days for symptoms of hypervitaminosis A, like excessive crying, raised fontanelle and vomiting.

Results

Seroconversion rates to types 1, 2 and 3 OPV viruses were 77.5%, 79.6% and 65.3% in the control group and were similar to the respective seroconversion rates of 67.3%, 83.6% and 63.3% observed in the experimental group. The geometric mean titers (\pm SD) of the antibodies at 6 weeks were 23.4 ± 3.47 ; 21.6 ± 2.8 and 9.7 ± 2.69 in the control group and 18.4 ± 2.94 ; 17.9 ± 3.19 and 9.6 ± 3.18 in the experimental group for types 1, 2 and 3, respectively and were comparable between the two groups at 6 weeks of age.

The percentage of infants having different levels of serum retinol in cord blood, along with their mean values are presented in *Table 1*. Eighty six per cent of the infants at birth had serum retinol $< 20 \mu\text{g/dl}$, while 59% had values $< 15 \mu\text{g/dl}$. Percentage of infants with either of these initial levels significantly decreased to a similar extent in both the control and experimental groups by the age of 6 weeks. Mean values

TABLE I—Serum Retinol Levels of Infants of Vitamin A Supplemented Mothers

Group (S. retinol µg/dl)	Control		Experimental	
	Initial	6 weeks	Initial	6 weeks
< 15	32 (64) 11.9±0.46	9 (18) * 25.8±2.33	27 (54) 9.8±0.69	9 (18) * 21.7±1.43
> 15	18 (36) 19.0±0.70	41 (82) * 23.0±2.21	23 (46) 21.0±1.01	41 (82) * 27.8±3.11
< 20	45 (90) 13.1±0.56	24 (48) * 24.9±1.80	41 (82) 12.9±0.79	20 (40) * 22.6±1.65
> 20	5 (10) 22.0±0.48	26 (52) * 24.0±5.30	9 (18) 25.5±2.15	30 (60) * 33.9±4.92

Values are Number, (Percentage) and Mean ± SE in that order in each horizontal column.

* P < 0.001 compared to the respective initial values

of serum retinol showed significant increase from cord blood levels to 6 weeks age values in all infants in both the groups.

Hospital stay of the newborns in both the groups was uneventful. Mean (± SD) increase in weight and height of the infants from birth to 6 weeks age was comparable between the groups with 1.2 ± 0.50 kg and 5.6 ± 1.63 cm and 1.4 ± 0.34 kg and 5.9 ± 1.63 cm, respectively for the control and experimental groups of infants.

Breast milk retinol levels at different periods of lactation are depicted in *Fig. 1*. In both the groups the levels showed a significant decline from the high values in colostrum as the period of lactation advanced and plateaued between 30 and 45 days of lactation. The mean retinol levels were, however, significantly higher in the experimental group from 10 days to 45 days and the levels were comparable between the groups by 90 days of lactation.

Discussion

In this study we found that only 14% of the infants at birth had serum retinol levels more than 20 µg/dl, a level which is considered as the cut off to define vitamin A status in older children and adults. Considering 30 µg/dl as the value suggesting ade-

quate level of circulating retinol in women at the time of delivery in this population(12) and also taking into account that the retinol levels at birth in the infants are about 50-60% of the maternal levels at the time of delivery(13), we considered less than 15 µg/dl as a level that would more appropriately define the state of deficiency in the newborns and young infants compared to older infants. According to this cut-off value, 59% of the infants at birth were found to have inadequate levels of circulating retinol, the number decreasing significantly ($p < 0.001$) from 64 to 18% in the control group and from 54 to 18% in the experimental group by 45 days of age. This improvement was also reflected by a significant increase in mean values of serum retinol. Administration of vitamin A to the lactating mother soon after delivery was not found to offer any additional benefit on the serum retinol levels of the breastfed infants at 6 weeks of age. Nevertheless, breastmilk retinol levels of the supplemented mothers were significantly higher though for a short period of 90 days and indicate higher intakes of vitamin A through breast milk by the infants in the experimental group. Earlier workers also did not demonstrate any rise in serum retinol levels following administration of 25,000 IU of

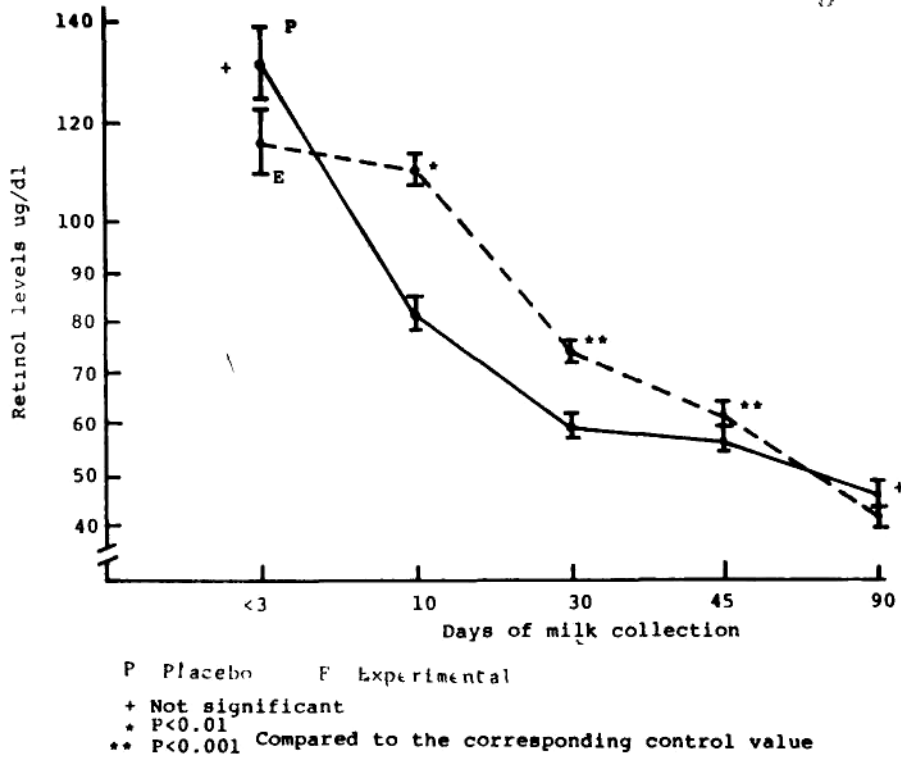


Fig 1 Breast milk Retinol Levels in Vitamin A Supplemented Mothers

vitamin A directly to infants at 6,10 and 14 weeks of age along with each dose of DPT vaccine(14) The reasons for lack of reflection of this higher intake of vitamin A on serum retinol levels are not clear but could possibly be due to the physiological immaturity of Retinol Binding Protein (RBP) synthesis by the young infants It is possible that the additional vitamin A could increase the hepatic stores

Postnatal follow up of infants in our study revealed no toxic effects due to the additional vitamin A intakes' through breastmilk, indicating the safety of such a procedure However, Rahaman *et al* observed significant bulging of anterior fontanelle in infants who received 25,000 IU directly(14) We observed no effect of the

maternal supplements on the growth of the infants

The adjuvant effects of vitamin A on immune response are well established(15) The effects of large dose of vitamin A in enhancing antibody titres when administered along with DT and measles vaccine have been demonstrated in our earlier clinical studies(7,16) In the present study we found that the vitamin A administered to mothers of breastfed infants had no significant effect on either the sero-conversion rates or the absolute antibody titres to OPV administered to the newborn The lack of immuno potentiating effect could be due to the relatively small increase in the intakes of vitamin A through breast milk by these infants, though the dose administered to

the mother is large. The effects of giving a large dose directly to the infants on the seroresponse to OPV could, however, be different but difficult to predict.

These observations suggest that maternal supplementation of large dose of vitamin A has no adverse effect on seroresponse to OPV. Further, OPV given to newborn had no adverse effects on the vitamin A status. In view of lack of evidence for positive beneficial effects on the biochemical vitamin A status or on the growth of infants, the recommendation of maternal vitamin A supplementation at the time of delivery to improve vitamin A status of breastfed infants needs to be reviewed.

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