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ORIGINAL CONTRIBUTIONS

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Effect of vitamin A supplementation on childhood morbidity and mortality

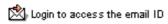
S Chowdhury, R Kumar, NK Ganguly, L Kumar, BN Walia

Community Medicine Department, PGIMER, Chandigarh 160012,

Correspondence Address:

S Chow dhury

Community Medicine Department, PGIMER, Chandigarh 160012





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Walia B N

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Intervention trials have shown that vitamin A supplementation reduces mortality by 23 to 30% among young children,[1],[2],[3]however, its effect on morbidity has been less clear. After vitamin A supplementation, some studies found no effect on illnesses [4],[5],[6],[7],[8],[9],[10],[11] whereas others have reported increased prevalence of diarrhoea and acute respiratory infections (ARI).[12],[13] It is possible that effect of vitamin A supplementation may manifest differently in different population groups depending on relative extent of vitamin A deficiency and other factors responsible for initiation, prolongation and outcome of infections. In most vitamin A trials vitamin.

A deficiency has been assessed clinically. Only few trials have estimated plasma retinol concentration in the study population [7],[10],[12] Therefore, we measured sub-clinical vitamin A deficiency status by conjunctival impression cytology (CIC) while studying the effect of vitamin A supplementation on childhood morbidity.

¤ Materials and methods

From three slums of Chandigarh, 1520 non-xerophthalmic children of less than 10 years of age were individually randomised in equal number to receive vitamin A or placebo. 2ml vitamin A (200000 I.U.) was given to children more than 12 months, 1 ml (100000 I.U.) to children aged 6-12 months and 0.5 ml (50000 I.U.) to less than 6-month-olds at every 4 to 6 months interval during the 15-month trial period. An equivalent volume of arachis oil was given as placebo. The family of four children in vitamin A group and one child in placebo group did not agree for dosing even after giving consent initially. Whenever signs/ symptoms of xerophthalmia developed appropriate therapy was given. Children who received a massive oral dose of vitamin A supplement from other sources were dropped from the study. In vitamin A group 604 (79.5%) and in placebo group 610 (80.3%) children were followed up regularly till

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the end of study.

Children were contacted every 15 days by home visits to obtain information on morbidity and mortality. The CIC with transfer as suggested by Luzeau et al [14]was done at an interval of two months among those who gave consent. Diarrhoea was defined as passage of 3 or more stools per 24 hours with altered (loose) consistency. If the episode of diarrhoea lasted more than 14 days it was labelled as persistent diarrhoea. ARI was defined as presence of cough for at least more than two days.

Pneumonia was defined as presence of fast breathing or chest-in-drawing in a child having cough. Measles case was defined when high fever (>38°C if measured) was reported with generalised rash lasting > 3 days in presence of at least one of the following symptoms: cough, coryza or conjunctivitis. A vernacular term 'Khasra' was used to inquire about measles cases. The signs and symptoms preceding death inquired and probable cause of death was assigned using verbal autopsy method.

Incidence of illnesses were calculated by dividing the number of episodes by the number of child-days at risk and 95% confidence interval (CI) for the relative risk (RR) was calculated according to Taylor Series Expansion method. Statistical differences in categorical variables were tested by Chisquare test or by Fisher's `exact test and differences in quantitative variables were tested by `t' test.

¤ Results

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The socio-demographic and anthropometric characteristics were found to be statistically similar in vitamin A and placebo group [Table - 1]. Following vitamin A supplementation changes in CIC started after two months [Table - 2] and thereafter, the prevalence of abnormal CIC in vitamin A supplemented children was significantly less (p<0.001) compared to placebo group. As shown in [Table - 3], incidence of diarrhoea, persistent diarrhoea and measles were significantly less in vitamin A group compared to placebo group. Incidence of ARI and pneumonia were similar in vitamin A and placebo group. The risk of death was also significantly reduced in vitamin A group (RR 0.14, 95% CI 0.030.63, p 0.006). There were 16 deaths during the follow-up period, two in vitamin A and 14 in placebo group. In the vitamin A group diarrhoea was the cause of death in both the children who died. In placebo group, causes of death were diarrhoea (6), chicken pox (1) fever (1), meningitis (2) pneumonia (3) and both diarrhoea and pneumonia in one child.

¤ Discussion

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The effect of vitamin A supplementation was studied in a homogeneous population with high prevalence of vitamin A deficiency where both the experimental and control groups were selected individually at random which is a better method for minimising the effect of confounding in comparison to the cluster randomisation. In earlier trials, only few had randomised children at individual level.[7],[10],[13]Children in the vitamin A supplemented group were similar to placebo group in every respect as shown in [Table - 1]. The number of children lost to follow up was similar in vitamin A and placebo groups. There were no significant differences in the socio-demographic characteristics between children who were followed up and those who dropped out (P>0.05).

Our study is the only one in which CIC was done during the trial to document the extent of sub-clinical vitamin A deficiency and to observe the change in CIC after vitamin A supplementation during the trial period. The prevalence of abnormal CIC decreased significantly in vitamin A supplemented children compared to placebo children [Table - 2]. This indicates that oral dose of vitamin A was absorbed and normal morphology of epithelial cells was restored in most children.

In our study the mortality in <10year-olds was significantly lower in vitamin A group (the upper 95% confidence limit shows at least 37% reduction). Beaton et all and Glasziou & MacKerras[2] have reported mortality reduction among young children exhibiting vitamin A deficiency at population level to the extent of 23-30% after vitamin A supplementation, however, the effect was found to be more pronounced for deaths due to diarrhoeal diseases, absent for ARI and detectable for measles. The effect on morbidity was considered to be less consistent. In our study incidence of diarrhoea and measles were found to be 38%% less in vitamin A supplemented children. The incidence of ARI and pneumonia after vitamin A supplementation were not statistically significant. Reduction in measles incidence by 54% in vitamin A supplemented group was a significant finding in our study. Some of the previous trials have also studied effect on measles incidence.[5],[6],[7],[8],[9],[10] However, measles cases in these studies were too few to draw a valid conclusion. The beneficial effect of vitamin A administration during measles illness for reducing case fatality is well established.[15]

Some studies have reported no reduction in morbidity after vitamin A supplementation [4][5][6][7][8][9][10][11] whereas others have reported increased morbidity. [12], [13] These deleterious effects were found mainly in children with adequate nutrition status but not in stunted children. This indicates that the physiological response to high dose of vitamin A may depend on the underlying vitamin A status of the child. In vitamin A deficient population the enhancement of non-specific immunity, maintaining physical and biological integrity of epithelial tissue as well as augmentation in specific immune response to infection is thought to be due to improved vitamin A nutriture. [1] So both the incidence as well as severity of infection may be expected to reduce after vitamin A supplementation. However, it is possible that the effect of vitamin A supplementation may manifest differently in different population groups depending on the relative extent of vitamin A deficiency and other factors responsible for initiation, prolongation and the outcome of infections. We observed a large reduction in diarrhoea) and measles morbidity

and cause mortality since the prevalence of vitamin A deficiency was quite high in our study community. Therefore, for prevention of morbidity and mortality among children promotion of vitamin A rich diet or supplementation with synthetic vitamin A at 4-6 months interval is required in populations where risk of vitamin A deficiency is high.

¤ Summary

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In a double blind design, 1520 children aged <10 years were individually randomised in vitamin A and placebo group in slums of Chandigarh. Children >12, 6-12 and <6 months of age received 200000, 100000, 500000 LU. of vitamin A respectively every 4 to 6 months during 15 months trial period. The prevalence of vitamin A deficiency was significantly reduced in vitamin A compared to placebo group during the follow-up period. In vitamin A group, incidence of diarrhoea and measles was significantly reduced but incidence of acute respiratory infections was not significantly different compared to control group. Risk of death was also significantly less in vitamin A group. Therefore, promotion of vitamin A rich diet or supplementation with synthetic vitamin A at 4-6 month interval should be a priority in populations where risk of vitamin A deficiency is high.

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Tables

[Table - 1], [Table - 2], [Table - 3]

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