

# Does Vitamin A Supplementation Help in Preventing Pneumonia?

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**L**ower respiratory tract infections (LRTI) are the leading cause of mortality in under-five children; most deaths occurring in South Asia and Africa. Vitamin A deficiency weakens the mucosal barrier to infection and its supplementation can plausibly prevent pneumonia. Considering the worldwide high burden of ARI, this systematic review aimed to assess the effectiveness and safety of vitamin A given to children up to seven years of age for its prevention.

## SUMMARY

Nine randomized controlled trials (RCTs) enrolling 33,179 children with LRTI (31,379 in the community and 1800 in hospital) were included; those including children with measles or HIV infection were excluded. Two trials were conducted in Indonesia whereas one each was from Brazil, India, Ghana, Congo, Mexico, USA and Canada. Six studies were mega-dose trials (100,000 to 200,000 IU vitamin A), and four were low-dose trials (5,000 to 45,000 IU vitamin A administered ranging from daily to every two months). The main outcome measures were incidence or prevalence of acute LRTIs defined on the basis of combination of fever, tachypnea, chest indrawing, cough, and chest signs. Megadoses of vitamin A failed to lower the incidence of acute LRTI [(RR 1.13, 95% CI 0.80-1.6) in community based trials ( $n=2$ ); and (RR 1.07, 95% CI 0.92 to 1.26) in a single hospital-based study ( $n=1$ )]. The low-dose trials ( $n=3$ ; two community based and

one hospital based) also could not demonstrate a protective effect of vitamin A on the incidence of LRTI. One trial showed that vitamin A had a significant protective effect on the incidence of acute LRTI in underweight children (RR 0.38, 95% CI 0.17 to 0.85), while it significantly elevated the incidence of acute LRTI in normal-weight children (RR 2.22, 95% CI 1.25 to 3.95). No study discussed the adverse effects of vitamin A. The authors concluded that vitamin A should not be given to all children to prevent acute LRTIs but may benefit those with low serum retinol or those with a poor nutritional status.

## COMMENTARY

*Are the results valid?*

The problem addressed in this review is relevant as mass supplementation with vitamin A is common in many countries and prevention of pneumonia is one of the oft-cited reasons in favor of this strategy. The authors searched the literature according to the Cochrane group's recommendations. In addition, authors actively searched Chinese studies from the Chinese Biomedicine Database (CBM). Surprisingly, all 25 Chinese articles claimed RCTs were found to be non-randomized (and therefore excluded from the review) when the authors of these studies were interviewed telephonically! It would have been interesting to note the results of the meta-analysis of these biased studies separately. The reasons for

**KEY MESSAGE**

- Vitamin A supplementation in children does not reduce the incidence of acute lower respiratory tract infections.

exclusion for some other studies are unclear from the report of this systematic review and should have been clearly mentioned in the flow chart. The methodological quality of the finally included studies was satisfactory. The heterogeneity was an issue because of the different dosages and treatment duration, definition of LRTI, and the duration of outcome assessment. The primary outcome of prevention of acute LRTI is functionally important but the WHO criteria used for defining the same in majority of studies have their own well-known limitations.

*How precise and clinically significant is the treatment effect?*

The total number of the subjects included in this review was quite large but a formal meta-analysis was not done for the primary outcome as a whole, probably because of the heterogeneity related to community based or hospital based studies, and low or mega doses of vitamin A. However, the meta-analyzed results from two large mega-dose trials involving over 2,500 children did not show any benefit of vitamin A supplementation in reducing LRTI, thus adding validity to this conclusion. The other conclusions, especially related to subgroup analysis with respect to nutritional status, are based on the results from single studies rather than a pooled estimate. The authors could have done some more

effort in segregating the results from the studies according to the nutritional status and combining them in form of a meta-analysis. This could have provided some useful and precise information on the issue of vitamin A supplementation in malnourished population. From a single study that reported benefit (in malnourished children) or harm (in normal children), the range of therapeutic benefit can not be calculated because of the logarithmic transformation of data on incidence. The conclusion related to benefit in children with low retinol level is baseless as no data related to this aspect has been provided in this review.

*Implications for Practice and Policy*

Vitamin A is often perceived as a magic bullet and its mass supplementation is promoted vigorously by International agencies. Evidence provided in this review suggests that vitamin A supplementation is not helpful for preventing pneumonia at least in normally nourished children and may rather worsen the situation. These results might force the policy makers of the countries to think twice before continuing or starting a universal vitamin A supplementation program. The adverse effects of vitamin A also need to be quantified from the ongoing supplementation studies or programs.

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