

Do We Need Universal Neonatal Vitamin A Supplementation?

Why are we obsessed with micronutrients as magic bullets for all remedies? As if they are the panacea for one and all ailments. From being remedial, these are now being projected as the shortcut to prevent our extinction! Zinc, folic acid, calcium, vitamin A, vitamin E, vitamin C, vitamin D—the list is swelling up. And now, Bhutta, *et al.*(1) put up an unconvincing case for supplementation of vitamin A during the neonatal period for the Asian region as a “core” intervention to improve infant survival!

Bhutta and his 10 co-authors identified three trials of vitamin A supplementation in the neonatal period in Asian population (Indonesia, South India, Bangladesh)(2-4) and reported that neonatal vitamin A supplementation was associated with a 21% reduction in mortality in babies younger than 6 months (random effects relative risk 0.79, 95% CI 0.65-0.96)(unpublished meta-analysis). The authors on one hand vociferously argued for utilizing only published data, yet used this unpublished meta-analysis to model vital estimates to bend the opinion of policy makers in favor of neonatal vitamin A supplementation(1). Negative data from other relevant trials from Asia(5) and Africa(6,7) were conveniently ignored. The inconsistency between the Asian and African regions also remains unexplained. Authors themselves agree “the disparate findings concerning the benefits of early newborn dosing from Africa and Asia without current biological explanation do concern us. These would merit further large-scale assessments in vitamin A deficient populations, to investigate the importance of potential effect modifiers such as HIV and malaria”(8); yet they were prompt enough to dole out a recommendation for an annual birth cohort of more than 50 million children, without enough evidence. The authors make a case for neonatal (<1 month) supplementation in the original review(1); however, in response to an embarrassing

correspondence(9) they justify their recommendation by restricting the evidence base to vitamin A supplementation within 3 days of birth(8). The review primarily makes the recommendation on the basis of ‘efficacy’ while ignoring other key elements of the decision tree analysis, especially safety, economics and logistics.

Icing on the cake was provided by HPS Sachdev, who despite being a co-author in the study, presented a separate meta-analysis of all available studies, which showed no evidence of benefit of neonatal vitamin A supplementation(9). He also claimed that the statement providing positive results of the unpublished meta-analysis was added without his prior knowledge(9). And that too, when Sachdev was specifically credited with the Vitamin A review for the paper(1). Bhutta, *et al.*(8) chose not to contest this in their response to Sachdev's letter (9). Also, only 5 of the ten other authors (excluding Sachdev) have responded in the reply(8), again raising a question whether the remaining 5 authors are in agreement with the recommendation of neonatal vitamin A supplementation. As a corollary, another important issue is whether one of the highest rated and prestigious journal (*The Lancet*) intends to do something about this transgression of publication ethics?

To have meaningful and holistic evidence, it is imperative to search for and include unpublished trials in any such analysis. For example, the largest ever randomized controlled trial—De-worming and Enhanced Vitamin A (DEVTA) trial in one million rural children in the state of Uttar Pradesh (UP) in north India is still unpublished. Half the children were given vitamin A and half were not. The mean probability that a 1 year-old would die by age 6 years was similar in the two groups [24.9 vs. 26 per 1000, respectively; RR 0.96 (99% CI 0.88-1.05)]. The study can make a major dent in the perceived role of vitamin A for improving child survival; if included in the meta-analysis results obtained till date. DEVTA and the other studies put together would show that vitamin A supplementation of older

children yields only moderate 11% (99% CI 6-16%) gain as compared to 23%(99% CI 12-33%) gain shown in the earlier analysis, done without incorporating this trial(10). The difference is almost double!

This controversy also shows that the quantitative research can also be presented in a subjective manner. Bhutta, *et al.*(1) have considered only nutrition-related interventions to improve selected nutritional outcomes or survival in mothers and children, based on numerical data. They have further not considered “several important interventions that might have broad and long-term benefits, such as education, untargeted economic strategies or those for poverty alleviation, agricultural modifications, farming subsidies, structural adjustments, social and political changes, and land reforms”(1). Probably there is a need for a qualitative analysis as well. This affirms my view expressed in the last editorial that “both quantitative and qualitative analyses put together only is likely to capture most of the reality, and provide holistic evidence”(11).

To conclude, it is essential to act urgently because there might be intense lobbying for initiating newborn vitamin A supplementation in the country. Even UNICEF and WHO may buckle to the pressure of this so called “core intervention”. Utmost caution is warranted against any hurried steps on the basis of this recommendation. Attempts could be under way to commercialize micronutrient malnutrition in the country by presenting incomplete evidence and my plea is that all the stakeholders should be aware of the complete evidence before any decision is taken.

There is no reason why we should only look up to the rest of the world to provide solutions to our problems. The world is looking to India, and its time that India recognizes the brilliance and mettle of her own sons and daughters. There is no dearth of heads with Einsteinonian IQ in this country. Need of the hour is to put them together and convince the policy makers to rely on the decision by our own.

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