Internal HKI Position Paper

Newborn Vitamin A Supplementation

Purpose: To summarize recent research findings on newborn vitamin A supplementation and provide guidance to HKI offices on contributing to further research and programs

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Summary

The reduction of infant mortality (death in the first year of life) has proven to be one of the more intractable public health challenges in the developing world. The consensus in the public health community is that we have reached a tipping point in the evidence for the efficacy of newborn\(^*\) vitamin A supplementation (NVAS) in reducing infant mortality in South Asia. Randomized control trials in Indonesia (Humphrey et al., 1996), Bangladesh (Klemm, 2008), and South India (Rahmathullah, 2003) have all shown significant reductions in infant mortality among those supplemented within 48 hours of birth with 50,000 IU of vitamin A (retinol) compared to control groups. In these settings the prevalence of vitamin A deficiency (VAD) remains high. A meta-analysis of these trials suggests that NVAS reduced the risk of death among infants up to six months by ~20 percent (West, 2007); conversely, a significant impact on neonatal mortality (death within 28 days after birth) has not been shown. A reduction in infant mortality has not yet been demonstrated in sub-Saharan Africa. Trials in Guinea-Bissau (Fisker, 2007) and Zimbabwe (Malaba, 2006) have failed to show reduced mortality, possibly because the settings chosen did not have high VAD or had high HIV seroprevalence; thus further research is still needed in this region. The World Health Organization (WHO) is not yet prepared to issue guidelines for NVAS and instead has been pursuing further debate and analysis of existing datasets. However, the U.S. Agency for International Development (USAID) and its partners are moving ahead with operational research in Nepal and Bangladesh to explore the optimal delivery mechanisms for newborn VAS and seek solutions to selected obstacles.

\(^*\) While medically the terms newborn and neonate are interchangeable, the use of the term newborn in this context is intended to refer to the timing within 48 hours of birth. The World Health Organization does not currently make this distinction.
Guidance

HKI country offices should support the advancement of NVAS by partnering with others to support operations research efforts in South Asian regions where efficacy research has demonstrated a survival benefit; and supporting further randomized clinical trials in Southeast Asia and the Pacific and sub-Saharan Africa.

More specifically, in the South Asian context this could include: i.) testing program delivery mechanisms; and ii.) advocacy to promote understanding of the current findings among key stakeholders in government, non-governmental, donor and academic sectors. In other sub-regions in Asia, HKI country offices could participate in any further research undertaken to document impact in new settings. In the African context our support could include: i.) supporting the conduct of randomized clinical trials in areas with VAD of public health importance and with low HIV seroprevalence (≤2 percent) to test the impact of NVAS on infant mortality; and ii.) interpreting the limitations of current findings and advocating for additional efficacy research among key stakeholders.

Rationale

The current strategies for improving vitamin A status among infants less than six months of age include post-partum vitamin A supplementation (VAS), promoting immediate and exclusive breastfeeding and increasing maternal access to and consumption of foods rich in bioavailable vitamin A, including vitamin A-fortified foods. At its 2001 meeting, the International Vitamin A Consultative Group (IVACG) presented recommendations, known as the “Annecy Accords,” for a revised schedule of maternal and infant supplementation. The schedule recommended for mothers included two post-partum doses of 200,000 IU (total 400,000 IU) to be delivered at least 24 hours apart as soon as possible after delivery, and no more than 6 weeks after. These recommendations were never incorporated by WHO into revised guidelines, and thus have not been widely disseminated†; consequently, most programs deliver just one dose to mothers. Nevertheless, rigorous research has demonstrated that post-partum maternal supplementation increased breast milk vitamin A concentration and reduced infant morbidity (Basu, 2003; Roy, 1997), but had no significant impact on infant mortality (Klemm, 2007). Maternal dosing has not been shown to bring infant VA status to adequate levels through 6 months of age. Supplementation during pregnancy with either low-dose VA or beta-carotene has also failed to demonstrate improved fetal or infant survival (Katz, 2000). By contrast, research in South Asian populations with high endemic vitamin A deficiency and high mortality have demonstrated that NVAS can significantly and dramatically reduce infant mortality. According to researchers at Johns Hopkins high coverage with NVAS could reduce the number of infant deaths in Southern Asia by as much as 200,000 annually (Tielsch, 2008).

† The Annecy accords also recommended supplementation of infants with three doses of 50,000 IU (at 6, 10 and 14 weeks in conjunction with the immunization calendar), but this schedule has also not been widely implemented.
Next Steps in Asia

South Asia
The research in South Asia strongly suggests that the mortality impact is strongest when infants are dosed within 48 hours of birth. In fact, the trial in India showed no significant impact among infants supplemented after 14 days of age, and in a trial in Nepal there was no significant impact from doses delivered between 1-5 months of age (West, 1995). An exception was the Bangladesh trial, which did show positive benefit even among infants supplemented nearly one month after birth (Klemm, 2008).

Efforts are underway involving USAID funding, and A2Z, Save the Children, Johns Hopkins University, CIDA and MI to design trials in 2-3 South Asian countries to test a range of delivery models. This operations research is likely to involve Nepal and Bangladesh. Key challenges will include the risks of confusion between newborn and post-partum supplementation doses and undermining messages about the harm of prelacteal feeds. Likely delivery mechanisms include household visits during home-based birth or post-partum by health workers or traditional birth attendants and female community health volunteers (TBAs/FCHVs) or clinic-based infant immunization visits, in particular coinciding with those for BCG (vaccination against tuberculosis) and/or polio. Ideally, efforts will be made also to link NVAS with post-partum supplementation. Achieving high coverage is likely to be a considerable challenge in light of the proportions of mothers who deliver at home without skilled birth attendants. HKI’s country offices in these two countries are urged to collaborate in these operations research studies as appropriate. HKI’s other APRO countries are encouraged to pursue similar opportunities for such high caliber collaboration in areas conducive to this research.

Next Steps in Sub-Saharan Africa

Thus far there is insufficient evidence of a mortality impact to support moving ahead with NVAS in this region. One explanation for the lack of evidence may be that trials to date have not been carried out in settings of high VA deficiency and high mortality rates (Tielsch, 2008). In addition, another recent study in Zimbabwe (Humphrey, 2006) showed a significant increase in mortality among supplemented newborns who were infected with HIV after 6 weeks of life, calling into question the safety of the intervention in HIV-endemic areas. Other possible confounders of the relationship between NVAS and mortality could be the prevalence of other infections such as measles and diarrhea, genetic factors such as infant sex, and vaccines given concomitantly with VAS, the timing and number of doses, and maternal vitamin A status (Abrams & Hilmers, 2008). HKI’s AFRO office has begun discussions with JHSPH about possible collaboration on a randomized community trial in this region; likely candidates where sufficient numbers of newborns could be enrolled include Mali and Tanzania.
Further Reading

The HKI intranet has a new link (http://intranet.hki.org/programs/nutrition/nutr_NVAS.html) that includes the key references cited in this policy paper, as well as trip reports describing the plans of A2Z for operations research in Bangladesh and Nepal and the Annecy statement. Also of special interest is the attached NVAS Frequently Asked Questions developed by the A2Z project.

For more information please contact:

Dr Jennifer Nielsen
Helen Keller International Headquarters
jnielsen@hki.org
References


