
**Introduction**

Iodine deficiency during early childhood can lead to irreversible damage of the developing brain and increase infant mortality. Salt iodization remains the strategy of choice to prevent iodine deficiency in populations (1); but in countries where iodized salt is not available or coverage is inadequate, the World Health Organization (WHO) recommends providing iodine supplements or iodine fortified complementary foods to pregnant and lactating women and infants, respectively (2). For lactating women, WHO, UNICEF, and the International Council for the Control of Iodine Deficiency Disorders (ICCIDD) recommend either a daily dose of 250 μg iodine as potassium iodide or one annual depot dose of 400 mg iodine as oral iodized oil, and exclusive breastfeeding for at least 6 months, on the assumption that breast milk will provide adequate iodine to the breastfed infant (2). However, this recommendation is based on studies in iodine-deficient pregnant women and other adults, and evidence is needed for the recommended strategy in lactating women.

This issue of NNA reports on a randomized clinical trial published in *The Lancet Diabetes & Endocrinology*. The study investigated the efficacy and safety of the existing WHO/UNICEF/ICCIDD recommendation for iodized oil supplementation of breastfeeding women and their infants by comparing two types of post-natal iodine supplementation strategies in Morocco. Although iodization of salt is mandatory in Morocco, compliance by the salt industry and enforcement of the regulations are poor (3). Thus, iodine deficiency remains prevalent in many regions of the country.

**Methods**

The study was a double-blind, randomized, placebo-controlled intervention trial in the Atlas Mountains of southern Morocco, where goiter used to be endemic (3). Healthy mother and infant pairs were recruited at a provincial hospital and were considered eligible if the infant was born full term, had a birth weight of at least 2.5 kg, was being breastfed (exclusively or partially) and younger than 8 weeks. The participants were considered ineligible if they had a history of major medical illnesses or thyroid dysfunction, long-term consumption of medication, or prior iodine supplementation during pregnancy or lactation.

A total of 239 mother and infant pairs were randomly assigned to one of two groups: 1) maternal supplementation, where the mother received 400 mg of oral iodine as 2 soft-gel capsules of iodized poppy seed oil and the infant received placebo oil; 2) infant supplementation, where the infant received about 100 mg of oral iodine as iodized poppy seed oil and the mother received 2 placebo capsules. These supplements were administered at baseline and again at 9 months. At baseline and when the infant was 3, 6 and 9 months old, spot urine and blood samples were collected, and infant weight, length and head circumference were measured. At 12 months, mental and psychomotor development was assessed in a sub-group using the Bayley Scales of Infant Development.
Results and Conclusions

Of the salt samples collected throughout the study period, 43% contained no iodine and an additional 51% were inadequately iodized, confirming that the salt iodization program had very low quality and low coverage in the study area.

Median age of mothers was 26 years and median age of infants was 2.0 weeks at the time of supplementation. At baseline, median urinary iodine concentration in mothers and infants was very low; 83% of women and 63% of infants had urinary iodine concentrations <100 µg/L, the cut-off for iodine deficiency. Provision of iodized oil to the mothers significantly increased maternal urinary iodine concentrations compared to placebo. But the median urinary iodine concentration in both groups remained <100 µg/L.

Exclusive breastfeeding was reported by 96% of mothers at baseline, 75% at 3 months, 66% at 6 months and 70% at 9 months. Breast milk iodine concentration in the infant supplementation group, in which mothers received placebo, gradually decreased from 43 µg/L (interquartile range (IQR) 25-71) at baseline to 26 µg/L (IQR 18-43) at 9 months. In the maternal supplementation group, in which mothers received iodized capsules, the breast milk iodine content significantly increased from baseline to 61 µg/L (IQR 36-95) at 3 months (p<0.0001) and was significantly higher throughout the study (49 µg/L (IQR 31-71) at 6 months and 39 µg/L (IQR 24-67) at 9 months) than in the infant supplementation group (p<0.0001). Because infants received iodine in both study groups (either directly from supplement or indirectly from breast milk), the urinary iodine concentration in infants increased significantly in both groups. However, in contrast to initial expectations, infants in the maternal supplementation group had higher urinary iodine concentration at 3 months (132 µg/L (IQR 70-259)) than in the infant supplementation group (99 µg/L (IQR 60-178); p=0.042). Infants in the maternal supplementation group were defined as iodine sufficient based on a median urinary iodine concentration >100 µg/L at 3 and 6 months, and marginally deficient at 9 month. The infants in the infant supplementation group were iodine sufficient at 6 months and marginally deficient at 3 and 9 months.

At baseline, 39% of infants had hypothyroxinemia (abnormally low thyroxin (T4) concentration in the blood) and 3% had overt hypothyroidism (defined as elevated thyroid-stimulating hormone (TSH) and abnormally low T4). The prevalence of these disorders significantly decreased in infants in both study groups (p<0.0001). Among the mothers, 12% had hypothyroxinemia at baseline. Providing iodized capsules to mothers in one of the groups did not have an impact on their T4 and TSH concentrations. There was also no difference in the prevalence of hypothyroxinemia between mothers who received iodized capsules compared to placebo. The authors reported that there were no serious adverse events in either of the study groups.

There were no significant differences in the anthropometric measurements between the two groups, except length-for-age z-score (LAZ) was slightly higher in the infant supplementation group. Development was tested in a sub-group at 12 months. Median mental and psychomotor development index score did not differ significantly from the expected median of a standard population and there were no group-wise differences for either score (p=0.685, p=0.477).

Program and Policy Implications

In summary, in a region of Morocco where iodine deficiency was moderate to severe despite a national salt fortification program, maternal supplementation of 400 mg iodine as iodized oil given to the breastfeeding mother soon after delivery resulted in significantly increased maternal urinary iodine, breast milk iodine and infant urinary iodine concentrations compared with direct infant supplementation with 100 mg iodine as iodized oil. Moreover, fewer infants had thyroid hypofunction in the maternal supplementation group. With indirect supplementation through breast milk, the infant received a small amount of iodine with each feeding, and this amount seemed to have been better absorbed than a large dose provided through iodized capsules. Because the study did not include a strict control group for ethical reasons, it is not possible to assess whether direct infant supplementation also had a beneficial impact on infants’ iodine and thyroid hormone status. The authors conclude that providing iodized oil capsules to breastfeeding mothers in regions of severe to moderate iodine deficiency is the more efficient strategy of iodine delivery to young infants.
breastfeeding children. However, they also note that the iodine status of the women did not reach sufficient levels, implying that further investigation is needed to develop safe approaches to ensure adequate iodine status of both infants and mothers.

NNA Editor’s Comments *

The above described study indicates that the recommendation by WHO and UNICEF (2) to provide 400 mg of iodine as iodized oil to lactating women is a safe and efficacious approach to increase iodine status of infants and their mothers in areas where iodized salt is not accessible. However, the iodine status of women remained deficient throughout the study period and infants were considered marginally iodine deficient at 9 months of age. It has to be noted, that an unusually high percent of participating mothers reported exclusive breastfeeding at baseline (96%) and even until the age of 9 months (70%) compared to the Demographic and Health Survey conducted in Morocco (4), suggesting that exclusive breastfeeding may have been over-reported. If these exclusive breastfeeding rates were real, it is uncertain whether maternal postnatal iodine supplementation would have the same impact in areas where exclusive breastfeeding rates are lower.

Considering the high prevalence of thyroid hypofunction in infants, the study highlights the importance of ensuring adequate iodine intake to prevent the detrimental effects of iodine deficiency. While efforts should continue to increase coverage and quality of salt iodization programs, WHO and UNICEF recommend considering iodine supplementation in countries and regions, in which less than 50% of households have access to iodized salt (2). This requires sub-national information to ensure identification of vulnerable population groups. Moreover, the rates of partial and exclusive breastfeeding have to be considered when deciding which approach would be most suitable. The authors suggest the first vaccination of infant immunization programs may be an ideal platform to provide iodized capsules to lactating women in countries or regions with inadequate salt iodization (3). Future research may also be needed to investigate safety, efficacy and feasibility of providing iodized oil capsules by the mid-wife immediately after birth. Research is also needed to determine the optimal dose of iodized oil in different settings.

*These comments have been added by the editorial team and are not part of the cited publication.

References
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