Direct or indirect iodine supplementation of infants?

Iodine is needed for thyroid hormone production and iodine sufficiency is particularly important during pregnancy, lactation, and infancy owing to the role of thyroid hormones in brain development. A deficiency of iodine during these life stages can result in impaired child cognition and has been associated with infant mortality. In countries with inadequate iodised salt coverage and iodine deficiency the WHO-UNICEF-International Council for the Control of Iodine Deficiency Disorders (ICCIDD) recommendation for infants who are exclusively breastfed and iodine-fortified complementary foods are not available, a supplement of 90 μg iodine per day or an annual dose of 200 mg is recommended. Surprisingly, these recommendations are based on little evidence, since no previous trial has examined whether such supplementation regimens are effective at improving infant iodine status and thyroid function, nor whether they are safe; this final point is important because infants are susceptible to iodine-induced hypothyroidism.

In The Lancet Diabetes & Endocrinology, Raschida R Bouhouch and colleagues report the results of their trial which aimed to assess the existing WHO-UNICEF-ICCIDD recommendations for iodine supplementation in lactation and infancy. They did a double-blind randomised controlled trial in which they compared two routes of iodine supplementation—either direct supplementation of the infant or indirect supplementation via the lactating mother. 241 mother–infant pairs were randomised to receive either one oral dose of iodised oil for the lactating mother (400 mg iodine) and placebo for the infant (indirect infant supplementation group) or iodised oil for the infant (100 mg iodine) and placebo for the mother (direct infant supplementation group). Despite the authors’ hypothesis that direct supplementation of iodine to the infant would be more effective at improving iodine status, the results show that infants in the indirect supplementation group had a greater increase in iodine concentration (p=0.042 for difference in urinary iodine concentration) over the course of the study, and a lower incidence of hypothyroxinaemia (p=0.026) in comparison with infants in the direct supplementation group. Why was indirect supplementation more efficacious than direct supplementation? The results of a substudy of eight infants who were closely monitored after receiving the direct 100 mg dose suggest that the iodine was poorly absorbed. It is likely that the iodine given via breastmilk provided the infant with a regular, more easily absorbed source of iodine.

One of the strengths of the study is the fact that mental and motor tests were done in a subgroup of infants at 12 months of age, thus assessing a functional outcome. The median values were not different to those of a reference population, but because there was no group in the study that did not receive iodine, the beneficial effect of iodine supplementation during infancy on neurological development cannot be truly ascertained. The proportion of infants with severe motor delay was higher in the study than would have been expected, which the authors attribute to the fact that the effects of in-utero iodine deficiency are not completely overcome by iodine supplementation in infancy. In view of the differences in infant iodine status and thyroid function between the indirect infant supplementation group and the direct infant supplementation group, it is perhaps surprising that there was no difference in mental and motor development scores. This could be because the substudy was not adequately powered; indeed, a lower proportion of infants in the indirect supplementation group (17.2% [ten of 58]), in which the individuals had overall better thyroid function and iodine sufficiency, had severe psychomotor delay than in the direct supplementation group (25.0% [14 of 56]), but the difference was not significant.

The results of the study by Bouhouch and colleagues support the existing WHO-UNICEF-ICCIDD recommendation that supplementation during lactation with 400 mg of iodine (as iodised oil) in countries with inadequate iodine nutrition can provide adequate iodine to breastfed infants for at least 6 months. Although direct supplementation of the infant did improve their iodine status and thyroid function, the results cannot
be used as evidence for the WHO-UNICEF-ICCIDD recommendations, because a lower dose was given (100 mg vs 200 mg). There was a much higher rate of exclusive breastfeeding at 6 months in the trial (65.3% [118 of 178]) than is prevalent in other countries, such as the UK or Australia where the rate is just 1% and 15%, respectively.4 A high dropoff rate for breastfeeding in many countries is another reason that indirect supplementation is preferable; if an infant receives a direct bolus dose of iodine during initial breastfeeding but then receives formula feed, which is generally fortified with iodine, there is potential for iodine overdose.

The results of the trial are particularly relevant to low-income countries where compliance is likely to be higher to one oral iodine dose than to a daily iodine supplement. However, in several countries daily supplementation with potassium iodide during lactation is recommended.5,6 Unfortunately the trial did not have a group to test the effectiveness of a daily supplement on maternal and infant thyroid function and neurological outcome. Such a trial still needs to be done, though the difficulty might be in obtaining ethical approval for a study which necessitates a placebo-controlled group.8 However, such a study might be possible in the UK since iodine supplementation in lactating mothers is not part of public policy.

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