Update / Le point

Safe use of iodized oil to prevent iodine deficiency in pregnant women*

A Statement by the World Health Organization[1]

The risks and expected benefits from iodized oil, given orally or by injection, to pregnant women in areas of severe iodine deficiency where iodized salt is not available were evaluated. The conclusions, which were approved by the International Council for Control of Iodine Deficiency Disorders (ICCIDD), showed that for preventing and controlling moderate and severe iodine deficiency, the giving of iodized oil is safe at any time during pregnancy. Maximum protection against endemic cretinism and neonatal hypothyroidism will be achieved when iodized oil is given before conception. The potential benefits greatly outweigh the potential risks in areas of moderate and severe iodine deficiency disorders, where iodized salt is not available and is unlikely to be made available in the short term (1–2 years).

Introduction

Since salt iodization is the optimal way of correcting iodine deficiency, it should continue to be the primary focus, through sustainable programmes, for preventing and controlling iodine deficiency disorders (IDD).[a] The level of iodization should be adjusted to provide the recommended dietary intake (RDI) of iodine in the quantity of salt usually consumed. For pregnant and lactating women the RDI for iodine is 200 µg/day (*1*).

Pending successful establishment of salt iodization in areas of moderate and severe iodine deficiency,[b] periodic large doses of iodine are frequently administered to all women of childbearing age, orally or by injection, in the form of slowly resorbable iodized oil. This intervention is an effective short-term public health approach that prevents goitre and iodine-related brain defects, including endemic cretinism, in children. There are, however, a number of doubts about the safety of using iodized oil, or daily doses of iodine far in excess of normal physiological need, to prevent IDD. For example, maternal iodine overload due to iodized oil during the crucial period of pregnancy could inhibit maternal thyroid function through a Wolff–Chaikoff effect,[c] thereby decreasing the availability of thyroxine to the fetus. Iodized oil could also directly affect fetal development. In addition, it has been suggested that iodized oil administered during late gestation could impair fetal and neonatal thyroid function, also through a Wolff–Chaikoff effect (*2*).

Responding to these concerns, the World Health Organization convened a group of experts to review and evaluate the results of programmes providing iodized oil to pregnant women. A careful review of the literature, and of experiences in several countries where iodized oil has been given at various stages of gestation, indicates that negative results

* A French translation of this article will appear in a later issue of the *Bulletin*.

[1] Based on a WHO Consultation on the Safety of Iodized Oil for Pregnant Women, Geneva, 13–14 September 1994. The participants at this meeting were Dr M. Benmiloud (*Chairman*), Algiers, Algeria; Dr F. Delange, Brussels, Belgium; Dr C.S. Pittman, Birmingham, AL, USA; Dr S. Yaffe, Bethesda, MD, USA; Dr C. Thilly, Brussels, Belgium; Dr C. Voumard, United Nations Children's Fund (UNICEF), Geneva, Switzerland. *WHO Secretariat*: Dr G. Clugston, Dr B. Underwood, Dr K. Bailey, and Dr J. Zupan. Requests for reprints should be sent to the Nutrition Unit, World Health Organization, 1211 Geneva 27, Switzerland.

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[a] *Iodine and health: eliminating iodine deficiency disorders safely through salt iodization.* A statement by the World Health Organization. Unpublished WHO document WHO/NUT/94.4, 1994 (available in English, French and Spanish).

[b] Moderate and severe iodine deficiency are defined in: *Indicators for assessing iodine deficiency disorders and their control through salt iodization.* Unpublished WHO document WHO/NUT/94.6, 1994 (available in English, French and Spanish).

[c] The Wolff-Chaikoff effect is the inhibitory effect exerted by excess iodine on the iodization of tyrosines in hormone synthesis.

have not been convincingly demonstrated.[d] The group concluded that, for purposes of preventing and controlling moderate and severe iodine deficiency, as defined by WHO,[b] the administration of iodized oil is safe at any time during pregnancy. Maximum protection against endemic cretinism and neonatal hypothyroidism will be achieved when iodized oil is given before conception. During the first trimester of pregnancy the supply of thyroid hormone to the human fetus appears to be critically dependent on maternal thyroid status. This relationship has been conclusively demonstrated in animals (*3*).

The group concluded that the available evidence conclusively demonstrates that iodized oil administered to women before, or at any time during, gestation has no harmful side-effects. Moreover, iodized oil not only prevents endemic cretinism and mental retardation in infants due to iodine deficiency, but also decreases fetal and perinatal mortality and increases the birth weight.

Prevention schedules and criteria

Dosage levels and frequency of administration, and the duration of protection expected from each are set out in Table 1. The dose selected and frequency of administration should be the lowest that will ensure protection throughout pregnancy, and during lactation for at least the first year postpartum. The dose that is compatible with the circumstances should be selected, and repeated if necessary, to ensure the desired degree of protection.

Table 1: **Dosage, frequency, and duration of effectiveness of administering iodized oil to fertile women of childbearing age**[a]

	Intramuscular[b]	Oral[c]	Oral[c]
Frequency, based on duration of effect	>1 year	12 months	6 months
Pregnant women	1 ml	300–480 mg	100–300 mg
Non-pregnant fertile women[d]	1 ml	400–960 mg	200–480 mg

[a] Adapted from the International Council for Control of Iodine Deficiency Disorders (ICCIDD).
[b] Lipiodol (ultra fluid): 1 ml contains about 480 mg iodine.
[c] Oriodol: 1 dose (0.57 ml) contains about 300 mg iodine. Lipiodol (capsule): 1 capsule (0.4 ml) contains about 200 mg iodine.
[d] Available data indicate that a dose of 100–200 mg orally protects for 3 months. No such data are available for pregnant women.

Criteria for giving iodized oil to pregnant women

Programme planners should carefully review the circumstances calling for the introduction or continuation of iodized oil supplementation programmes. The use of iodized oil for pregnant women and women of childbearing age should be considered only in situations where:

- the prevalence of iodine deficiency disorders is classified as moderate or severe;
- cretinism and neonatal hypothyroidism are present; and
- universal salt iodization programmes will not reach women of reproductive age within 1–2 years (which usually occurs in small areas within countries or regions, thus requiring area-specific interventions).

The reasons why iodized salt will not be available within a year or two should be thoroughly investigated before selecting iodized oil as a public health intervention. Sometimes salt iodization programmes in highly endemic areas cease functioning for unavoidable reasons. Should they be unable to restart soon, iodized oil may serve as a useful temporary measure.

Monitoring

The decision to use iodized oil for women of childbearing age should be made wherever the above criteria are met. Assessment of these criteria these requires baseline information on the distribution and severity of IDD, and on the availability of iodized salt throughout the area, country or region concerned. Assuming that the necessary baseline information is available, a monitoring system is required to evaluate both the programme's efficiency and its biological effectiveness. The system should include sufficient numbers of pregnant women to provide valid data for evaluation purposes and should be established within the context of national IDD control programmes.

Optimal biological and process indicators for effective monitoring of programmes to prevent fetal brain damage using iodized oil are given below.

Biological indicators. These apply to infants and mothers.

[d] See article on pages 99—106 of this issue of the *Bulletin* (**Delange F.** Administration of iodized oil during pregnancy: a summary of the published evidence).

• *Infant*

— birth weight;

— perinatal mortality rate;

— neonatal serum thyroid-stimulating hormone (TSH).

• *Mother*

— urinary iodine concentration;

— breast-milk iodine concentration.

At least one of the indicators should be neonatal TSH or maternal urinary iodine.

Process indicators. These include the following:

— availability of iodized oil at distribution points;

— system in place for registering and tracking the doses given;

— proportion of a programme's eligible subjects seen antenatally who have received iodized oil;

— system in place to determine pregnancy outcomes.

Conclusion

Based on the available scientific and programmatic evidence, the proposed iodized oil prevention schedule in this statement will lead to no detectable adverse effects on human health. The potential benefits to be derived greatly outweigh the potential risks in areas of moderate and severe IDD prevalence where iodized salt is not available, and is unlikely to be made available in the short term, i.e., within 1–2 years.

References

1. *Trace elements in human nutrition and health.* Geneva, World Health Organization (in press).
2. **Kochupillai N et al.** Iodine deficiency and neonatal hypothyroidism. *Bulletin of the World Health Organization*, 1986, **64**: 547–551.
3. **Morreale de Escobar G et al.** Hormone nurturing of the developing brain: the rat model. In: Stanbury JB, ed. *The damaged brain of iodine deficiency.* New York, Cognizant Communication Corp., 1994.