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Iodised Oil Injections in Goitre Prophylaxis

Possible Impact on the Newborn

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In 1973, we published evidence to show that more than half the goitrous subjects in a severely iodine deficient environment can be functionally decompensated as evidenced by the TRH test (Kochupillai *et al., Lancet,* 1.1021,1973). This finding raised questions of concern regarding thyroid status of newborns in iodine deficient regions. The question was of importance particularly because of the recognised role of thyroid hormones in brain development and the irreparable nature of brain damage caused by untreated hypothyroidism early in life.

To address this question we developed appropriate field methods and RIA techniques and successfully organised a screening programme for neonatal chemical hypothyroidism (NCH) in the Gonda and Deoria districts of Uttar Pradesh and reported four percent to 13 percent incidence of NCH in these regions (Kochupillai *et al., Endocrinology,* 102, 128, 1978; *Ind. Jour. Med. Res.,* 80.293, 1984). Efficacy of iodised oil injections in pregnancy in improving neonatal thyroid status in endemic goitrous regions had been reported in literature (Thilly *et al., Jour. Clin. Endocrinol. Metab.*, 47.354, 1978). Because of this, and concerned by the high risk of brain damage due to neonatal thyroxine deficiency in these areas, we initiated a pilot iodised oil injection programme, as an emergency measure of prophylaxis, in some of the areas of our study with high incidence of NCH. Also we organised a careful follow-up study to assess the impact of the prophylactic programme, using a variety of parameters including cord-blood hormone levels of newborns, and breast milk iodine content of mothers who had had iodised oil injections.

Methods

Assessment of severity of iodine deficiency: Severity of iodine deficiency in a given area was assessed by determining the pattern of urinary iodine excretion in the total population as per criteria defined by Follis (Group I: no individual excretes less than 50 μg iodide per gram of creatinine; Group V: majority of individuals excrete less than 25 μg iodide per gram of creatinine). Random urine samples were collected in tightly stoppered wide-mouthed, iodine-free polythene bottles in which toluene was added as preservative. Urinary iodine estimation was done by the alkali ash method, with minor modifications. Total iodine content of breast milk was also determined by a modified alkali-ash method. Urinary creatinine was estimated by the alkaline picrate method.

Iodised oil prophylaxis: One ml. Lipiodol given intramuscularly was the method chosen for the prophylaxis programme. Children of school going age groups and women of reproductive age groups, including pregnant mothers, were the major target populations. A total of over 12,000 injections were given in three weeks' period. A representative sub-set of these groups of populations were followed up annually for assessing urinary iodine excretion pattern (UIE) and goitre grade, among them. Mainly children of school age were studied for goitre and UIE pattern studies. Pregnant mothers who received injection mostly in the antenatal clinic of PHCs and sub-centres were carefully followed up to assess the cord-blood hormone status of their newborn babies, as well as the breast milk iodine content after delivery.

Hormone assays: T_4 and TSH were assayed in cord-blood sera of babies born to mothers who had had iodised oil injection, in the various antenatal clinics, during their pregnancies. Cord-blood samples were collected at birth, sera separated and stored under ice before it reached the laboratory at Delhi. T_4 was measured in the sera by specific and sensitive RIAs developed and validated in our laboratory. TSH was measured by reagents kindly supplied by the National Institute of Health, Bethesda (Parlow's antiserum). T_4 standard was obtained from M/s Henning Berlin Gmbh and TSH standard was the WHO reference standard. The inter and intra assay co-efficient of variation of the two RIAs did not exceed eight percent.

Results

The overall prevalence of goitre in the district of Deoria was 80 percent. Three to five percent cretinism was observed in the seriously goitrous flood-prone villages of the district. However, goitre prevalence was less severe and cretinism absent in most villages which were not flood-prone. The urinary iodine excretion pattern observed in the areas of study could be categorised as belonging to grade V of Follis' Classification.

Sixty to 70 percent goitre prevalence was observed in the villages studied from Gonda district. Cretinism was pre-

sent in several flood affected villages of these districts while there were also villages with less goitre prevalence and no cretinism. The UIE pattern observed in both these areas could also be categorised as Follis' group V.

At 30 months after iodised oil prophylaxis, iodide excretion pattern observed among the population under prophylaxis could be categorised as belonging to Follis' group I, indicating continued state of satisfactory iodine availability two-and-a-half years after the depot injection. As compared to this satisfactory state of iodine availability in the study population, the control population, which was not given the iodised oil injection, continued to show severe iodine deficiency as indicated by urinary iodine excretion pattern classifiable as Follis' group V. Consistent with this observation of satisfactory iodine availability was the significant decline in goitre prevalence recorded in the population under prophylaxis. There was no noticeable decline in the goitre prevalence among the control population during this period.

Studies on iodine content of breast milk of mothers who had had iodised oil prophylaxis during pregnancy also showed relatively higher iodine content to ensure adequate iodine availability to the newborns, if breast feeding was practiced.

Thyroid status of newborns: Though the above results were encouraging from the point of view of the efficacy of iodised oil injection as a measure of goitre prophylaxis, *the results of studies on thyroid status of newborns given birth by mothers who had had iodised oil prophylaxis during pregnancy told a different story*. A total of 154 babies born to mothers who had had iodised oil prophylaxis during pregnancy could be studied for their cord-blood T_4 and TSH levels. Sixteen of these newborns had neonatal chemical hypothyroidism as per criteria adopted by us ($T_4 < 3.0$ μgram/dl and TSH > 50 μu/ml.). The mean duration before delivery, when iodised oil injection was given to these mothers was 3.5 weeks. The table gives details of data in this regard. *These data indicate that iodised oil injection, when given to mothers particularly in the last trimester of pregnancy, does not help reduce the incidence of neonatal chemical hypothyroidism in iodine deficient environments.*

Discussion

The results of our studies on iodised oil prophylaxis in the Gonda and Deoria districts, detailed above, can be summarised as follows:

- 1 ml. Lipiodol injections given intramuscularly as prophylaxis to iodine deficient population help maintain satisfactory UIE pattern in the population for as long as 30 months and also help reduce the prevalence of goitre in the population.
- Iodised oil injections given prior to pregnancy can help improve the breast milk iodine content, and thus help curb iodine deficiency in neonates.
- As much as 10 percent of babies born to mothers who have had iodised oil injection during the last trimester of pregnancy, showed neonatal chemical hypothyroidism, as per criteria adopted by us ($T_4 < 3.0$ μg/dl; TSH > 50 μu/ml.).

High incidence neonatal chemical hypothyroidism has been reported from endemic areas of India and elsewhere. These reports have helped to re-focus attention from endemic goitre to neonatal hypothyroidism related impairment of brain development as the major health problem in iodine deficient environments, where over 400 million people are estimated to be living in Asia alone. As a result of this recent realisation, there has been a new momentum, created in the implementation of iodine prophylactic programmes in developing countries with significant problems of environmental iodine deficiency. Of the available methods of iodine prophylaxis, iodised oil injection is regarded next only to salt iodation in efficacy and cost-effectiveness. Indeed, in remote and inaccessible endemic regions which are socio-economically poor and backward, the depot mode of prophylaxis provided by iodised oil injection is progressively being promoted as the method of choice. However, the efficacy of iodised oil has largely been demonstrated only in terms of reduction in goitre prevalence, and prolonged improvement in the status of iodine availability to the population as reflected in the UIE pattern, but not in terms of its impact on hypothyroidism in the newborns.

In view of the recent perception that neonatal thyroid failure, and consequent impairment of brain development of emerging generations, is about the most important public health concern in iodine deficient regions, it is important to assess the impact of any iodine prophylactic programme using the yardstick of reduction in incidence of NCH. In particular, it is all-important to assess this parameter in the poverty stricken malnourished endemic populations, because there is indirect evidence to believe that neonatal chemical hypothyroidism and malnutrition, early in life, may act synergistically to cause irreversible brain damage (Ramalingaswami & Kochupillai, *Iodine Nutrition, Thyroxine and Brain Development*, Tata McGraw Hill, 1986).

Our observations on the effect of iodised oil injection in pregnancy on neonatal thyroid status is at variance with those reported by Thilly *et al.* (loc. cit.), who had claimed improved thyroid status on a set of babies born to mothers given iodised oil *at or before the fifth month of pregnancy*. In our programme, iodine prophylaxis was given mostly to expectant mothers in the last trimester of pregnancy. This is the time when they frequently attend the antenatal clinics of primary health centres and in public health practice this is the time when most pregnant women can be reached. In such a situation, we found that more than 10 percent newborn, 16 of the 154, given birth by mothers who had had iodised oil prophylaxis, were hypothyroid at birth.

In view of the differences in our observations and those of Thilly *et al.*, it is important to consider the possible reasons thereof. As has already been mentioned, the major difference between our studies and those of Thilly *et al.* is that, whereas Thilly *et al.* gave iodised oil dur-

Table: Neonatal Chemical Hypothyroidism Among Babies Born to Mothers Who Had Iodised Oil Injections

Mode of maternal prophylaxis	1 ml. iodised oil I.M
Number of newborns studied	154
Number of hypothyroid newborns detected	16 (10.4%)
Mean interval between injections and delivery	3.5 weeks