

# IMPACT OF IODIZED OIL INJECTION DURING PREGNANCY ON THYROID FUNCTION TESTS OF OFFSPRINGS

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## ABSTRACT

Previous studies have shown that injection of iodized oil in pregnant women can be used as a prophylactic strategy for iodine deficiency disorders and may improve the growth indices of their offspring. Since administration of pharmacological doses of iodine may lead occasionally to large goiter and rarely to hypothyroidism, in the present study the thyroid function tests of neonates and infants born to women who had received 480 mg iodized oil intramuscularly during pregnancy were assessed and compared to those of a control group.

Of 277 cord blood samples obtained from Mazandaran and Khohkiluyeh-Boyerahmad provinces, 125 made up the case (injected) and 152 the control (non-injected) group. Of 1026 blood samples of the neonates and infants from Mazandaran province, 544 made up the case and 482 the control group. Serum  $T_4$ ,  $T_3$  and TSH concentrations were measured with RIA kits.

In the cord blood samples, mean serum  $T_4$  in cases who had received iodized oil was lower than that of the control group:  $140 \pm 32$  vs.  $149 \pm 33$  nmol/L, respectively;  $p < 0.03$ .  $T_3$  and TSH were not however different. In the neonates and infants,  $T_4$  and  $T_3$  concentrations were significantly higher in the case than control group:  $178 \pm 40$  vs.  $168 \pm 39$  and  $3.5 \pm 0.02$  vs.  $3.0 \pm 0.02$  nmol/L, respectively, both  $p < 0.001$ . In contrast, TSH concentrations were lower in the experimental group in comparison to control:  $2.6 \pm 2.2$  vs.  $3.1 \pm 2.9$  mU/L, respectively;  $p < 0.001$ . Increased  $T_3$  and decreased TSH were seen in infants of mothers who were injected in the second and third trimesters of pregnancy.

Injection of iodized oil in pregnant women does not cause hypothyroidism in the offsprings, however it does cause a transient increase in serum thyroid hormones and a decrease in TSH concentrations.

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## INTRODUCTION

For over thirty years, iodized oil has been successfully used for the prevention and treatment of iodine deficiency disorders (IDD).<sup>1</sup> Although iodized salt consumption has been successfully employed in the pro-

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phylaxis of IDD,<sup>2</sup> iodized oil administration is recommended in severely deficient regions with mental and growth retardation or hypothyroidism.<sup>3-7</sup> Prophylaxis of endemic cretinism<sup>8,9</sup> and neonatal hypothyroidism will only be achieved when iodized oil is administered before conception and during pregnancy.<sup>10,11</sup>

Not only does iodized oil prevent endemic cretinism<sup>12-14</sup> and mental retardation<sup>15-17</sup> but it also decreases fetal and perinatal mortality<sup>18-20</sup> and increases birth weight<sup>21-23</sup>. Previous studies demonstrated that iodized oil administration to women before, or at any time during gestation was safe<sup>24</sup> and devoid of adverse effects for the pregnant mother.<sup>25</sup> However, it is well known that the fetal thyroid may be unable to avoid the Wolff-Chaikoff phenomenon.<sup>26-28</sup> It has been demonstrated that exposure to high doses of iodine in pregnant women may cause goiter and hypothyroidism in their newborn.<sup>30-32</sup>

Goiter, physical and intellectual growth retardation have been prevalent in the Islamic Republic of Iran<sup>33-35</sup> and attempts to control IDD have been made by universal salt iodization.<sup>36</sup> In the national program for control of IDD in Iran, iodized oil was administered to people residing in the hyperendemic regions.<sup>4</sup> Two provinces of Mazandaran and Kohkiluyeh-Boyerahmadi were covered in this national program. This study was conducted in 1993-94 in order to assess the effect of iodized oil injection in pregnant women on the thyroid function of their offsprings in these two provinces.

## SUBJECTS AND METHODS

A 1989 national survey of goiter in the Islamic Republic of Iran showed that goiter prevailed in schoolchildren in most provinces at a rate of between 30-80%<sup>7</sup> and it was estimated that some 20 million people were at risk of iodine deficiency. Iran's National Committee for Control of IDD (NCC-IDD) was established in 1989. The production and distribution of iodized salt, with 40 mg of potassium iodide per kg of sodium chloride and the education of policymakers, health personnel and public was begun in 1990. However, a rapid survey of iodized salt consumption in 1993 showed that less than 40% of the households in rural areas consumed iodized salt with a mean urinary iodine from 5.0 to 8.2 mg/dL in spot locations. Therefore, NCC-IDD decided to use iodized oil prophylaxis for areas with goiter prevalence of over 30% in schoolchildren.

Schoolchildren of Mazandaran and Kohkiluyeh & Boyerahmad provinces had severe iodine deficiency with total goiter rate of 90 and 67% respectively in the previous national survey in 1989.<sup>33</sup> Urinary iodine excretions in the 2 locations were 33.6±36.1 (median 31.2) and 24.0±16.6 mg/L (median 23.2).<sup>37</sup> Therefore, all inhabitants of the rural regions in both provinces were included in

the national program of iodized oil supplementation.

Six hundred sixty nine healthy pregnant women from endemic rural regions of Mazandaran and Kohkiluyeh-Boyerahmad received one milliliter containing 480 mg iodized oil (Lipidol, Laboratory Guerbet, France) intramuscularly. Controls were randomly selected among non-injected (at the time of this study) pregnant women's infants. We studied 277 cord blood samples, 125 in the case (injected) and 152 in the control (non-injected) groups. We also took 1026 blood samples from the neonates and infants, for up to 12 months of age, 544 in the case and 482 in the control groups. Complete data in 62, 79 and 170 infants whose mothers received iodized oil injection during the first, second and third trimesters, respectively, were available. The date of iodized oil injection during pregnancy and the age of the neonate were recorded. In all subjects, whole blood was obtained, centrifuged and serum frozen immediately and transported to the central laboratory of the Endocrine Research Center.

Serum T<sub>4</sub>, T<sub>3</sub> and TSH concentrations were measured with commercial radioimmunoassay (RIA) kits (Amersham, UK). The intra-assay and interassay coefficient of variations were both below 10%. This study was approved by the Ethics Committee of the Endocrine Research Center.

Results were expressed as mean±SD. Student's t-test and ANOVA were used to compare the means between groups. Statistical significance was determined at the  $p < 0.05$  level of confidence.

## RESULTS

### Cord blood

Serum T<sub>4</sub> concentration was marginally but significantly lower in the experimental group when compared to the control: 140±32 vs. 149±33 nmol/L, respectively,  $p < 0.03$ . There was no statistical difference in T<sub>3</sub> and TSH concentrations between the experimental and control groups: 0.86±0.48 vs. 0.92±0.48 nmol/L and 6.7±5.5 vs. 6.9±5.3 mU/L, respectively. Serum TSH concentration in cord blood samples was more than 20 mU/L in 5 and 6 of iodized oil injected and control mothers, respectively. Serum T<sub>4</sub>, T<sub>3</sub> and TSH concentrations of cord blood samples in those who had TSH over 20 mU/L are shown in Table I. There is no statistical difference in T<sub>4</sub>, T<sub>3</sub> and TSH concentrations between the two groups.

### Neonates

Mean serum T<sub>4</sub> and T<sub>3</sub> concentrations were significantly higher in the experimental group as compared to the controls: T<sub>4</sub>; 178±40 vs. 168±39,  $p < 0.001$  and T<sub>3</sub>; 3.5±0.02 vs. 3.0±0.02 nmol/L respectively,  $p < 0.001$ . Mean serum TSH concentration was lower in the children of

injected subjects as compared to the control group:  $2.6 \pm 2.2$  vs.  $3.1 \pm 2.9$  mU/L, respectively,  $p < 0.001$ . Serum concentrations of  $T_4$ ,  $T_3$  and TSH were compared in various groups of infants aged <1, 2, 3, 4, 5 and >6 months of age. Table II shows serum  $T_4$ ,  $T_3$  and TSH concentrations in neonates and infants whose mothers received iodized oil in the first, second and third trimesters of pregnancy and controls. There is no significant difference in  $T_4$ ,  $T_3$  and TSH concentrations between infants whose mothers were injected with iodized oil in the first trimester of pregnancy, and infants of the control group. Serum  $T_3$  showed an increase and serum TSH a decrease in infants whose mothers were treated with iodized oil in the second and third trimesters of pregnancy when compared to control infants. Serum  $T_4$  was also increased in these infants, but it was statistically significant only in infants of mothers injected in their third trimester.

In infants whose mothers received iodized oil during the second trimester of pregnancy, serum  $T_3$  was higher and serum TSH was lower than in controls in infants less than one month of age:  $3.9 \pm 0.3$  vs.  $2.5 \pm 0.2$  nmol/L ( $p < 0.001$ ) and  $2.7 \pm 0.36$  vs.  $4.4 \pm 0.29$  mU/L ( $p < 0.02$ ), respectively. Serum TSH was also significantly decreased in the second months of life, as compared to infants of the control group:  $1.8 \pm 0.28$  vs.  $2.9 \pm 0.25$  mU/L,  $p < 0.013$ . Serum  $T_4$  in infants <1 to 6 months old and serum  $T_3$  in 2 to 6 months old and serum TSH levels in 3 to 6 months old infants of this group were not significantly different from controls.

Fig. 1 shows serum  $T_4$ ,  $T_3$  and TSH concentrations in infants whose mothers received iodized oil during the third trimester of pregnancy. Serum  $T_4$  was significantly increased in the below one and 2 month old infants; serum  $T_3$  was increased in the second one, 3, 4, and 5 months old infants; serum TSH was decreased in 2 and 3 months old infants, as compared to control infants. Serum  $T_4$ ,  $T_3$  and TSH concentrations in infants whose

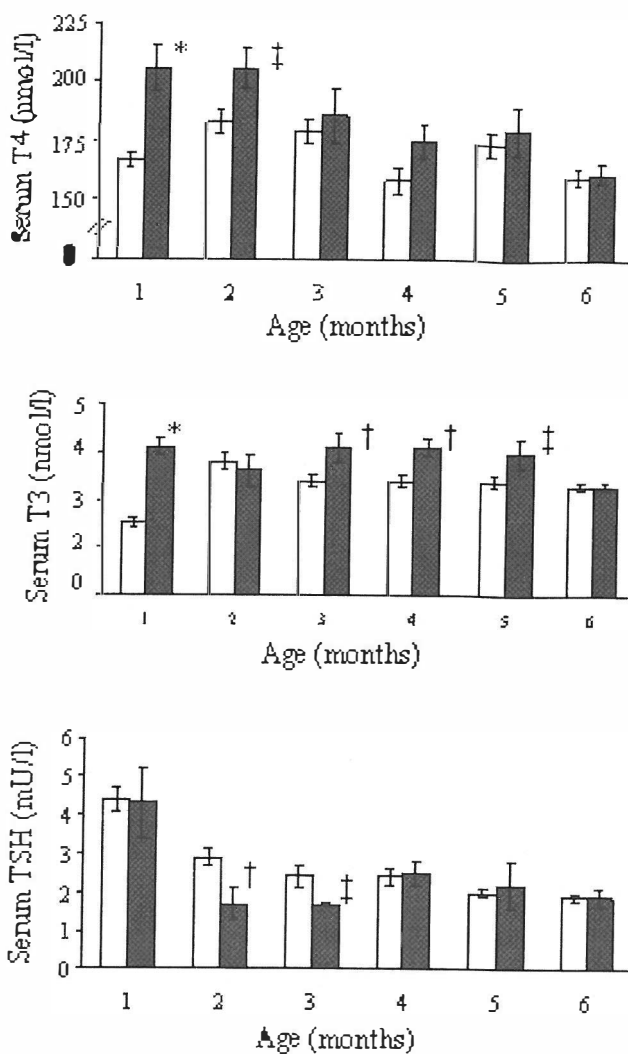


Fig. 1. Serum  $T_4$ ,  $T_3$  and TSH concentrations in neonates and infants whose mothers received 480 mg iodized oil in the third trimester of pregnancy (case) and control neonates and infants. \* $p < 0.001$ , † $p < 0.02$ , ‡ $p < 0.04$ , compared to control group.

Table I. Serum  $T_4$ ,  $T_3$  and TSH concentrations of cord blood samples of case and control mothers who had TSH of more than 20 mU/L.

Groups		$T_4$ (nmol/L)	$T_3$ (nmol/L)	TSH (mU/L)
Case	1	91	0.61	41
	2	151	1.08	23
	3	167	1.08	21
	4	145	1.02	25
	5	192	0.53	23
Control	6	115	0.77	33
	7	116	1.38	22
	8	129	1.67	23
	9	117	0.61	39
	10	206	2.61	21
	11	133	0.62	24

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