Effect of passive smoking on thyroid function in infants

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Abstract

Objective: To evaluate the effect of passive smoking on thyroid function in infants.

Design and methods: Cord serum tri-iodothyronine (T3), free T3 (fT3), thyroxine (T4), free T4 (fT4), TSH, thyroxine binding globulin (TBG), thyroglobulin (TG) and cord plasma thiocyanate were measured at birth, and serum TG and thiocyanate after 1 year of life, in 18 infants born from parents who did not smoke (group A), in 18 infants with a father who smoked (group B) and in 18 infants with parents both being smokers (group C).

Results: No significant differences were observed in cord serum concentrations of T3, fT3, T4, fT4, TSH and TBG among the three groups. Median (range) TG concentrations (ng/ml) were 30.2 (5.0-102.0), 56.3 (20.5-208.0) and 76.0 (26.0-199.0) at birth ($P=0.009$ for groups A and B compared; $P=0.0002$ for groups A and C compared), and 14.9 (5.4-32.0), 19.5 (10.0-57.5) and 20.0 (14.0-40.7) at 1 year ($P=0.017$ for groups A and C compared), in the three groups respectively, and thiocyanate concentrations (mmol/l) were 3.3 (0.0-51.4), 12.9 (0.0-122.2) and 27.8 (3.3-184.5) at birth ($P=0.015$ for groups A and C compared), and 3.1 (0.0-32.7), 6.0 (0.0-47.3) and 20.3 (0.0-30.8) at 1 year ($P=0.01$ for groups A and C compared) in the three groups respectively.

Conclusions: TG and thiocyanate concentrations at birth and at 1 year of age in infants of smoking parents are greater than in infants with non-smoking parents. These results indicate that the change in thyroid function as evaluated by serum TG concentrations observed at birth can persist at least for 1 year if the exposure to passive smoking from both parents is continued. Increased TG concentrations may be due to a direct effect of thiocyanate on the thyroid gland.

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Introduction

Several researchers have evaluated the negative effects of exposure to cigarette smoke during pregnancy on the fetus and reported a correlation with low birth weight and increased frequency of respiratory disease and learning or behavioural problems. The causes have not been completely identified and remain the subject of investigation (1–4).

The habit of smoking can affect thyroid function. Thiocyanate, derived from hydrogen cyanide, leads to increased excretion of iodine, seems to inhibit iodine uptake by the thyroid, and can have a goitrogenic effect in the presence of iodine deficiency (5–7).

In view of the significant correlation that has been reported between cord blood concentrations of thiocyanate and thyroglobulin (TG) (5), suggesting a direct effect of thiocyanate on the thyroid gland, our aim was to follow infants to 1 year of age, in order to explore the hypothesis that an altered thyroid function can persist in consequence of protracted exposure to passive smoking.

Subjects and methods

We investigated three groups of children, born in the Section of Neonatology of our Division of Neonatal Intensive Care during a 4-month period: group A comprised 18 infants with mean (± S.D.) birth weight 3251 ± 311 g, born to parents who did not smoke and were not exposed to smoke either at home or at work; group B were 18 infants with mean birth weight 3296 ± 353 g, with a smoking father and a non-smoking mother; group C were 18 infants with mean birth weight 2985 ± 373 g, whose parents both were smokers. Group B were included to evaluate the risk for the fetus of the exposure of the non-smoking mother to passive smoking.

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All the mothers were healthy and none of them developed postpartum thyroiditis. All the infants were born at term (gestational age 39–41 weeks), after normal pregnancy and delivery, had birth weights appropriate for gestational age and Apgar scores of 9 or 10 at 5 min. Infants with malformations, prematurity or other severe diseases were excluded from the study, as were infants born after complicated pregnancy or delivery, as mode of delivery can influence TG concentrations (8).

Smoking parents consumed at least 10 cigarettes per day (more than 180 packs per year) during gestation and the first year after delivery. No significant factors besides smoking habit, such as socio-economic status, work environment or type of feeding, were noted that could influence exposure to thiocyanate in the parents of the three groups of infants.

After informed consent was obtained from the parents, samples were collected of maternal blood (2 ml) to exclude contamination, cord blood (2 ml) and peripheral blood of the child at 1 year of age (1 ml). Serum tri-iodothyronine (T₃), free T₃ (fT₃), thyroxine (T₄), free T₄ (fT₄), thyroid-stimulating hormone (TSH), thyroxine-binding globulin (TBG) and TG and plasma thiocyanate concentrations were measured in cord and mother’s blood; when the children were 1 year of age, thiocyanate concentrations were measured in cord and infants’ thyroid hormone concentrations.

Birth weight was significantly lower in infants with smoking parents than in controls or infants with only a father who smoked (P=0.026).

No significant differences in growth and development among the three groups were found during follow-up at 1, 6 and 12 months of age. No alterations of the sleep–wake rhythm or irregularity of the alvus were observed in either breast- or formula-fed infants.

Results

Assay for anti-thyroglobulin antibodies gave negative results in both infants and mothers. No significant relationships were observed between mothers’ and infants’ thyroid hormone concentrations.

No significant differences were observed in the concentrations of T₃, T₄, fT₃, fT₄, TSH and TBG in the cord blood of the three groups, but the concentrations of TG were significantly lower in group A than in groups B (P=0.009) and C (P=0.0002).

Thiocyanate concentrations in cord blood did not differ between groups A and B, whereas group C had higher concentrations than group A (P=0.015).

At 1 year of age, the differences between serum TG concentrations remained significant only between groups A and C (P=0.017). Similarly, thiocyanate concentrations at 1 year of life were significantly different between groups A and C (P=0.01), but not between groups A and B.

No significant differences in growth and development among the three groups were found during follow-up at 1, 6 and 12 months of age. No alterations of the sleep–wake rhythm or irregularity of the alvus were observed, in either breast- or formula-fed infants.

Discussion

Several authors have reported the presence of metabolites of nicotine in adults and children exposed to passive smoke (12–14). Among the metabolites, the influence of thiocyanate on thyroid function has received...
Thyroglobulin is a large glycoprotein that functions as a reservoir for the thyroid hormones and their precursors. Furthermore, it binds several iodized molecules: aminoacids (mono-iodothyronine and di-iodothyronine), iodized dipeptides, proteins such as iodoalbumin, and others. It is released in small amounts from the thyroid into the circulation. Low serum concentrations of TG are usually found in infants with thyroid dysgenesis or defects of TG synthesis or secretion; undetectable TG usually indicates thyroid aplasia, whereas a finding of TG in the serum indicates that functional thyroid tissue is present. Increased concentrations have been observed in different thyroid disorders and are considered an excellent marker for recurrence of thyroid tumour in patients taking thyroxine. TG does not cross the placental barrier and the concentrations are greater in cord blood than in maternal blood, although the explanation for this finding remains to be clarified. Our results confirmed the gradual reduction of TG concentrations during the first year of life that has been reported by others (8).

The present study confirmed the increased concentrations of cord TG in the infants of smoking parents as previously reported by Chanoine et al. (5); this increase was accompanied by increased concentrations of thiocyanate in group C compared with group A. Furthermore, it seems that the exposure of the pregnant woman to passive smoking by her partner resulted in a significant passage of the metabolites of nicotine through the placenta, as group B also demonstrated increased concentrations of TG and thiocyanate in cord blood.

The difference in TG concentrations between groups A and C persisted 1 year after birth, whereas it was no longer evident between groups A and B. This was in accordance with the changes in thiocyanate concentrations. It seemed that, if the period of exposure to passive smoking was prolonged, the alterations in TG concentrations persisted. Interestingly, the difference was observed only when the exposure to paternal smoking at home was added to that of the mother. Possible explanations of the lack of difference between groups A and B 1 year after birth could be that, if the father was smoking he smoked at a considerable distance from the child, or that only an intense exposure to passive smoking from both parents may produce a significant effect on thyroid function.

These findings could be related either to chronic sympathetic stimulation induced by nicotine, or to a direct effect of thiocyanate on thyroid cellular function (20).

Several studies have reported an increased prevalence of goitre in smokers. This was associated with an increase in serum TG and thiocyanate concentrations (7). The increase in the thyroid volume/birth weight ratio observed in newborns appeared to parallel the increase in cord serum thiocyanate concentrations found in infants of smoking mothers, suggesting that

### Table 1 Cord blood serum thyroid hormone and thiocyanate concentrations in the three groups of infants. Values are median and range.

<table>
<thead>
<tr>
<th>Group</th>
<th>T3 (ng/ml)</th>
<th>T4 (µg/dl)</th>
<th>IT3 (pg/ml)</th>
<th>IT4 (pg/ml)</th>
<th>TSH (U/ml)</th>
<th>TBG (µg/ml)</th>
<th>TG (ng/ml)</th>
<th>Thiocyanate (µmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td>0.5</td>
<td>9.3</td>
<td>1.5</td>
<td>10.0</td>
<td>4.5</td>
<td>33.7</td>
<td>30.2</td>
<td>3.3**</td>
</tr>
<tr>
<td>(n = 18)</td>
<td>0.2–1.7</td>
<td>5.7–11.4</td>
<td>1.2–2.5</td>
<td>8.7–11.4</td>
<td>1.7–12</td>
<td>11.3–54.6</td>
<td>5.0–102.0</td>
<td>0.0–51.4</td>
</tr>
<tr>
<td>Group B</td>
<td>0.6</td>
<td>9.5</td>
<td>1.4</td>
<td>9.2</td>
<td>6.7</td>
<td>35.5</td>
<td>56.3</td>
<td>12.9</td>
</tr>
<tr>
<td>(n = 18)</td>
<td>0.3–6.1</td>
<td>7.6–15.7</td>
<td>1.1–1.9</td>
<td>8.0–12.2</td>
<td>3.0–47.5</td>
<td>25.5–66.2</td>
<td>20.5–208.0</td>
<td>0.0–122.2</td>
</tr>
<tr>
<td>Group C</td>
<td>0.5</td>
<td>9.7</td>
<td>1.5</td>
<td>9.6</td>
<td>4.9</td>
<td>35.5</td>
<td>76.0</td>
<td>27.8</td>
</tr>
<tr>
<td>(n = 18)</td>
<td>0.3–0.7</td>
<td>5.0–12.4</td>
<td>1.1–1.9</td>
<td>8.2–11.7</td>
<td>3.0–13.5</td>
<td>23.9–48.4</td>
<td>26.0–199.0</td>
<td>3.3–184.5</td>
</tr>
</tbody>
</table>

*P = 0.009 compared with group B and P = 0.0002 compared with group C; **P = 0.015 compared with group C.

### Table 2 Serum thyroglobulin (TG) and thiocyanate concentrations in the three groups of infants at 1 year of age. Values are median and range.

<table>
<thead>
<tr>
<th>Group</th>
<th>TG (ng/ml)</th>
<th>Thiocyanate (µmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td>14.9*</td>
<td>3.1**</td>
</tr>
<tr>
<td>(n = 14)</td>
<td>5.4–32.0</td>
<td>0.0–32.7</td>
</tr>
<tr>
<td>Group B</td>
<td>19.5</td>
<td>6.0</td>
</tr>
<tr>
<td>(n = 16)</td>
<td>10.0–57.5</td>
<td>0.0–47.3</td>
</tr>
<tr>
<td>Group C</td>
<td>20.0</td>
<td>20.3</td>
</tr>
<tr>
<td>(n = 10)</td>
<td>14.0–40.7</td>
<td>0.0–230.8</td>
</tr>
</tbody>
</table>

*P = 0.017 compared with group C; **P = 0.01 compared with group C.
smoking during pregnancy may be a relevant cause of thyroid gland enlargement in the newborn (5), probably by reducing iodine availability (7).

As no significant influence of parental smoking on the development and growth of the children was observed, study of the effects of passive smoking on thyroid function should be extended to older children, in order to evaluate whether a relation exists between altered thyroid function and behavioural problems observed in children exposed to passive smoking (21, 22). The clinical picture observed in adolescents exposed to passive smoking could be due to direct stimulation of sympathetic nervous activity induced by nicotine, superimposed upon the smoking-induced increase in thyroid hormone secretion (8).

Acknowledgements

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References