

Iodine and hypothyroidism in neonates with congenital heart disease

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Abstract

Aim—To evaluate the influence of the intravenous injection of iodine during cardiac catheterisation, and of topical iodine antiseptics during surgical procedures, on thyroid function in full term neonates.

Methods—Twenty one full term infants with major cardiac anomalies who survived for more than a month were studied. Thyroxine and thyrotropin concentrations were measured (by radioimmunoassay) before each procedure, 24 hours after the procedure, and every week thereafter until the age of 1 month or until normal. Thyroxine values less than 64.4 nmol/l were considered low, while thyrotropin values greater than 30 mU/l were considered high.

Results—Thyroid function tests before iodine exposure were within normal limits in all infants. Following catheterisation or surgery six infants had raised thyrotropin concentrations; three had low thyroxine concentrations. Two of those infants were treated with L-thyroxine.

Conclusion—Iodine exposure during cardiac catheterisation or surgery may induce transient hypothyroidism in term infants.

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Keywords: iodine; hypothyroidism; cardiac malformations; catheterisation

Thyroid disorders from an excess of iodine may result from direct ingestion, absorption from the skin and mucous membranes, or from administration of organic iodine containing compounds such as radiological contrast agents.¹ The purpose of this study was to evaluate prospectively the influence of the intravenous injection of iodine during cardiac catheterisation and exposure to topical iodine containing antiseptics during surgical procedures, on the thyroid function of full term neonates with major congenital cardiac malformations.

Methods

The Chaim Sheba neonatal intensive care unit is a tertiary referral centre for infants with major congenital cardiac malformations. Twenty one consecutively admitted term neonates with major cardiac anomalies (mean (SD) gestational age 39.2 (1.1) weeks and birthweight 2670 (320) g) who had survived for more than a month were studied. Table 1

details the characteristics of the cardiac anomalies and the number of cardiac catheterisations and surgical procedures during which they were exposed to iodine.

During each cardiac catheterisation 1–3 ml/kg of Optiray 300 (Laboratoire Guerbet, France) was administered. The topical antiseptic used during surgical procedures was povidone-iodine 1%, swabbed three times over the entire chest area. Blood samples for thyroxine (T₄) and thyrotropin (TSH) measurements were spotted on to filter paper before each procedure, 24 hours afterwards, and every week thereafter until the age of 1 month or until normal T₄ and TSH values were reached. The first urine specimen obtained after every procedure was processed for urinary iodine measurements. If this sample was not available a sample was obtained within six hours of the procedure being accepted.

T₄ and TSH concentrations of blood spotted on to filter paper were measured using radioimmunoassay (neonatal T₄ and TSH, Diagnostic Product Cooperation, Los Angeles, CA, USA). T₄ values less than 64.4 nmol/l were considered low (range of normal 64.4–231.7 nmol/l), while TSH values greater than 30 mU/l were considered high (range of normal 1–25 mU/l). Iodine measurement in urine was performed by modification of the Sandell-Kolthoff reaction described by Dunn *et al*² and Wawschinek *et al*.³ Basically, the reaction was produced by digesting urine with chlorate, followed by a catalytic reduction by iodine of Ce(SO₄)₂·2(NH₄)₂SO₄·2H₂O in the presence of arsenious acid. The reaction product was monitored spectrophotometrically at 405 nm.

Results

Thyroid function tests before iodine exposure were within normal limits in all infants. Between two and 24 days afterwards (catheterisation or

Table 1 Number of cardiac catheterisations and surgical procedures

| Diagnosis | No of infants | No of catheterisations | No of surgical procedures | Total no of procedures |
|-------------|---------------|------------------------|---------------------------|------------------------|
| Coarctation | 4 | 5 | 4 | 9 |
| TGA | 3 | 2 | 3 | 5 |
| PS/PA | 10 | 8 | 8 | 16 |
| VSD | 1 | 1 | | 1 |
| TA | 1 | 1 | 1 | 2 |
| TOF | 1 | 1 | | 1 |
| ASD+AV | | | | |
| Fistula | 1 | 1 | 2 | 3 |
| Total | 21 | 19 | 18 | 37 |

PS pulmonary stenosis; PA pulmonary atresia; TGA transposition of great arteries; VSD ventricular septal defect; TA tricuspid atresia; TOF tetralogy of Fallot; ASD atrial septal defect; AV fistula-arteriovenous fistula.

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Table 2 Infants with abnormal thyroid function tests following cardiac catheterisation or surgery

| Diagnosis | Catheterisation age (days) | Surgery age (days) | *Age (days) | T ₄ (nmol/l) | TSH mIU/l (lowest) | Follow up |
|-------------|----------------------------|--------------------|-------------|-------------------------|--------------------|-------------------------|
| VSD | 15 | | 25 | 117.1 | 69 | Normal at 55 days |
| TGA | 1 | 2 | 15 | 139.0 | 89 | Lost to follow up |
| Coarctation | 2, 10, 57 | 4, 59 | 15 | 82.3 | 60 | Normal at 63 days |
| PS | 2 | 14, 15 | 15 | 82.3 | 63 | Normal at 37 days |
| PS | 2 | 7, 14 | 4 | 51.5 | 27.9 | Normal at 22 days |
| Coarctation | 2 | 5 | 26 | 48.9 | >200 | Treatment for 10 months |
| TOF | 2 | | 9 | 27.0 | 110 | Treatment for 6 months |

*Age at which disturbed thyroid function first noted; PS pulmonary stenosis; PA pulmonary atresia; TGA transposition of great arteries; VSD ventricular septal defect; TA tricuspid atresia; TOF tetralogy of Fallot; ASD atrial septal defect; AV fistula-arteriovenous fistula.

surgery), six infants had raised TSH values (>30 mU/l), three of whom also had low T₄ values (<64.4 nmol/l) (table 2). In four of these infants thyroid function tests were normal at the age of 22 to 63 days, while two infants required L-thyroxine treatment for six and 10 months, respectively. The decision to treat these infants with thyroxine was based on both low T₄ and high TSH values. There were no significant differences between the seven infants with disturbed thyroid function tests and the 14 infants who had normal thyroid function tests in terms of birthweight, gestational age, days of mechanical ventilation, days of oxygen treatment or incidence of sepsis. The concentration of iodine found in the urine of the 21 infants ranged between 55 000 to 1200 000 µg/l (normal concentration <100 µg/l in our population). The seven infants with abnormal thyroid function tests underwent a mean of 2.4 procedures compared with 1.4 procedures in infants with normal tests, but this difference was not significant by Student's *t* test (table 1).

Discussion

Exposure to large amounts of iodine induced hypothyroidism in term infants undergoing cardiac catheterisation or surgical procedures. Transient hypothyroidism has been reported in babies undergoing cardiac catheterisation, with a decline in total T₄ values from baseline for at least seven days after the procedure, which was associated with a transient increase in TSH.⁴ Transcutaneous iodine absorption in infants undergoing cardiac operation has also been reported.⁵

The phenomenon of transient hypothyroidism caused by exposure to high doses of iodine is known as the Wolff-Chaikoff effect.⁶⁻⁸ A mature thyroid gland is supposed to escape from inhibition after about 48 hours.⁷ This escape phenomenon normally develops during the neonatal period. Delay in the development of autoregulation and impaired organic iodine formation in the neonatal period accounts for iodine induced hypothyroidism in infants exposed to large amounts of iodine.⁹⁻¹¹

The presence of low T₄ caused by adaptive depression of thyroid function in term neonates with severe illness or haemodynamic complications is difficult to differentiate from pathological iodine induced thyroid dysfunction.

An increase in TSH is the most important diagnostic tool for this differentiation.

In this study it was impossible to differentiate between the relative contribution of intravenous iodine administration and topical iodine absorption. In addition to the iodine injected during catheterisation, significant quantities of iodine from topical disinfection may have been absorbed, due to the relatively small amount of subcutaneous tissue¹² and a higher surface area:weight ratio in neonates.¹³ The number of procedures performed tended to be higher in the cases where thyroid dysfunction was found, possibly reflecting a dose related effect, but a significant association between the dose of iodine administered and thyroid dysfunction was not found.

In conclusion, iodine absorption from iodine containing contrast agents during cardiac catheterisation or from iodine containing topical antiseptics may cause disturbances in thyroid function in full term infants. As thyroid hormones have an important role in the normal neurological development of infants, this transient disturbance in thyroid function may be detrimental. It is thus recommended that attempts should be made to reduce the amount of iodine used during procedures and to carefully monitor thyroid function in all neonates exposed to an excess of iodine.

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