Thyroid hormone metabolism in pediatric cardiac patients treated by continuous povidone–iodine irrigation for deep sternal wound infection

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1. Introduction

Deep sternal wound infection (DSWI) is a devastating postoperative complication following median sternotomy in children with congenital heart defects. Povidone–iodine is frequently used for continuous mediastinal irrigation as it is a very effective antiseptic agent. However, the use of povidone–iodine may be without adverse effects. It has been shown that the use of iodine antiseptics [1,2] or contrasts agents [3] in infants may lead to transient thyroid dysfunction. High concentration of exogenous iodine decreases thyroid hormone synthesis. Infants may not overcome this blockade, thus exogenous iodine may produce hypothyroidism with its negative impact on neurodevelopment. Iodine-induced hyperthyroidism is rare and has been described in a newborn with povidone–iodine continuous mediastinal irrigation [4].

The present study was undertaken to evaluate prospectively the effect of povidone–iodine continuous mediastinal irrigation on thyroid function in infants and children.

2. Materials and methods

The study was approved by the Local Ethics Committee at Children’s University Hospital, Bratislava, Slovakia.

Between 1992 and 1999, 23 patients (1.5%), of the 1565 patients undergoing cardiac operation through midline ster-
notomy at our institution, developed DSWI. DSWI was defined according to the guidelines of the Centers for Disease Control and Prevention [5]. The diagnosis of DSWI was confirmed if patient met at least one of the following criteria: (1) sternal instability with evidence of mediastinitis seen during operation; (2) purulent discharge from the mediastinum; (3) an organism isolated from blood culture and/or culture of drainage; (4) clinical signs of infection (fever, pain, irritability, inadequate peroral intake). The most common cardiac diagnoses were single-ventricle lesions (9 pts), ventricular septal defects (6 pts), and tetralogy of Fallot (4 pts).

All patients with clinical and laboratory signs of DSWI were managed using a consistent protocol including sternal debridement, removal of foreign materials, closed mediastinal irrigation with povidone–iodine solution, and antibiotic intravenous treatment.

The operative field was painted with 10% aqueous povidone–iodine (Betadine, EGIS Pharmaceuticals Ltd., Budapest, Hungary) and skin was covered by an iodophor adhesive drape (Ioban 2, 3M Health Care, St. Paul, MN, USA). After extensive sternal debridement and removal of foreign materials, the mediastinum was repeatedly irrigated with warm 0.5% povidone–iodine solution. Two sump drains and one irrigation catheter were placed in the mediastinum and sternum was closed with stainless steel wires. The presternal space was obliterated with one layer of absorbable suture and skin was closed with subcuticular non-absorbable suture.

Postoperatively, the mediastinum was irrigated continuously with povidone–iodine solution, at a rate of 20 ml/h and simultaneously drained by gentle suction (−20 cm H₂O). On postoperative day (POD) 1, povidone–iodine solution at a concentration of 0.05% was used, on POD 2 the concentration was decreased to 0.01% and on POD 3 to 0.005%. Then the povidone–iodine irrigation was stopped and the drainage tubes were removed.

If the suspicion of reinfection arose, patients underwent another mediastinal reexploration followed by debridement procedure and povidone–iodine irrigation for the duration of 6 days. A concentration of 0.05% of povidone–iodine was used on POD 1–2, 0.01% on POD 3–4 and 0.005% on POD 5–6.

The measurement of thyroid hormones was done in 18 pediatric cardiac patients treated with continuous povidone–iodine irrigation for postoperative DSWI. The median age of patients was 8 months (18 days–5.3 years). The study population consisted of one newborn, 14 infants and three children. The median time from the primary operation to the onset of clinical and laboratory signs of infection was 9 days (3–37). In three patients, the suspicion of reinfection arose 5 days (4–6) after the discontinuation of povidone–iodine irrigation.

Sample serum levels for thyroid hormone evaluation were obtained from indwelling venous catheters at these points: (a) prior to mediastinal reexploration (before povidone–iodine exposure); (b) immediately after discontinuation of povidone–iodine irrigation; (c) 2 weeks after discontinuation of mediastinal irrigation. In patients with repeated mediastinal irrigation, data immediately and 2 weeks after last exposure to povidone–iodine were analyzed. Serum was separated and frozen and samples were analyzed for total triiodothyronine (TT₃), total thyroxine (TT₄), free triiodothyronine (FT₃), free thyroxine (FT₄), thyroid-stimulating hormone (TSH), reverse triiodothyronine (rT₃) and thyroxine-binding globulin (TBG). TT₄ and TT₃ were measured by RIA methods (ImmunoTech, Czech Republic). Normal reference ranges in our laboratory were 1.23–3.0 nmol/l for TT₃, 116–203 nmol/l for TT₄ in newborns more than 4 days of age and 57–154 nmol/l in infants and children. FT₃ and FT₄ were assayed by RIA methods (Brahms Diagnostica GmBH, Germany). Normal values for FT₃ ranged from 3 to 9 pmol/l in newborns and from 3.5 to 6.5 pmol/l in infants and children. Reference ranges for FT₄ were 14–28 pmol/l in newborns and 9–20 pmol/l in infants and children. TSH was measured by IRMA (ImmunoTech, Czech Republic), the normal range being 0.32–4.5 mIU/l. Serum rT₃ and TBG were determined by RIA kits (Biocode, Belgium) with normal values of 15–35 ng/dl for rT₃ and 12–26 μg/ml for TBG.

A sample of urine for measurement of iodine concentration was obtained on the last day of povidone–iodine exposure, immediately after discontinuation of povidone–iodine irrigation, then frozen and analyzed. Urinary iodine concentration was examined by inductively coupled plasma mass spectrophotometry (ICP-MS, Analytica, Czech Republic).

2.1. Statistical analysis

Data are expressed as the median (range) in text and 10th, 25th, 50th, 75th, and 90th percentiles in figures. Kruskal/ Wallis and Wilcoxon tests are used to test the difference between the hormone levels prior to mediastinal reexploration (sample 1) and after discontinuation of mediastinal irrigation (samples 2 and 3). Mann–Whitney test was used to compare ioduria between the patients with continuous povidone–iodine irrigation and the group of healthy infants. The level of significance was set at P < 0.05. Statistical analysis was undertaken with JMP software (version: 4.0.2).

3. Results

3.1. Thyroid hormone evaluation

The median serum values of TT₃ and TT₄ (Fig. 1) were prior to mediastinal reexploration below the normal range. TT₃ and TT₄ levels increased significantly during mediastinal irrigation and over the next 2 weeks to concentrations within the normal range.

The median serum FT₃ levels (Fig. 2) were within the normal range throughout the observation period, though a significant increase of FT₃ levels was observed during the
period of 2 weeks after discontinuation of irrigation. The median serum FT4 concentration (Fig. 2) was within the normal range prior to irrigation and did not change significantly.

Prior to mediastinal irrigation, the median rT3 level (Fig. 3) was within the normal range, but close to upper limit. During irrigation, the median rT3 level slightly decreased. The median TBG levels (Fig. 3) were within the normal range throughout the observation period, though a significant increase of TBG levels was observed during the period of mediastinal irrigation.

The median TSH level (Fig. 4) was within the normal range prior to mediastinal irrigation and did not change significantly.

3.2. Ioduria

Urinary iodine concentration was evaluated on the last day of iodine exposure. In patients with povidone–iodine irrigation, urinary iodine concentrations were significantly higher 6700 µg/l (range, 1600–15 000 µg/l) than in the group of 53 healthy infants 200 µg/l (range, 20–780 µg/l, P < 0.001).

4. Discussion

Povidone–iodine is a very effective antiseptic agent. However, its use may be associated with thyroid disorders, especially in newborns and infants.

The patients with DSWI are exposed to povidone–iodine at several steps – preoperative disinfection of skin, an iodophor adhesive drape during surgery, povidone–iodine irrigation after debridement procedure and continuous povidone–iodine mediastinal irrigation after chest closure.

Transcutaneous absorption of iodine with large increases in serum and urinary iodine concentrations has been demonstrated in infants who were undergoing thoracic or closed cardiac procedures [6–8]. Absorption of iodine across mediastinum was demonstrated in experimental study. Glick et al. [9] found that during continuous mediastinal irrigation with povidone–iodine, iodine is absorbed rapidly
across the serous membranes of the mediastinum. The rate of absorption is a function of the irrigation rate and the irrigant concentration. The exclusive route of elimination is renal, with the rate of iodine excretion being proportional to the serum iodine concentration at any given time.

Our study revealed high urinary iodine concentrations in all patients with povidone–iodine irrigations. In this study, however, it was impossible to determine the relative contribution of transcutaneous absorption and absorption of iodine across mediastinum. Although high urinary iodine concentrations suggest significant iodine absorption, laboratory data on thyroid hormone status have not revealed any significant thyroid disorder. Thyroid dysfunction has not been even noticed in patients with reinfection who required repeated and prolonged mediastinal irrigations.

Prior to mediastinal reexploration, low TT3, TT4 and high rT3 levels were recorded in most of our patients. During the mediastinal irrigation, TT3 and TT4 levels significantly increased and rT3 levels slightly decreased. The findings of low TT3, TT4 levels and high rT3 levels in the patients with DSWI may represent changes that usually occur in critical non-thyroidal illnesses (Euthyroid Sick Syndrome) [10]. Thyroid hormone alterations that occur in children after cardiac surgery may also contribute to these findings [11–13].

The most important laboratory sign of hypothyroid state is increased value of TSH. Frequently, it is accompanied by decreased level of FT4. Our data showed FT4 levels prior to mediastinal irrigation being within the normal range in all patients. In four patients, FT4 levels increased slightly during irrigation and the next 2 weeks thereafter returned to the normal range. TSH levels prior to irrigation were within the normal range in all but one patient. During the period of irrigation, TSH levels increased in three patients to concentrations being above upper normal limit. However, over the next 2 weeks following that period, TSH in these patients decreased to concentrations within the normal range. The patient with high baseline TSH level also showed an increase of TSH level during irrigation. Over the next 2 weeks, TSH level declined, but its value remained above upper normal limit. The further check-up in 2 weeks showed the level being within the normal range. Transient hyperthyrotropinaemia we have found in our patients has been also described in newborns exposed to povidone–iodine for umbilical cord care [14,15] and in newborns with congenital heart defects after surgery or catheterization [3]. No patient showed laboratory signs of iodine-induced hypothyroidism (persisting high TSH levels, low FT4 levels).

5. Conclusions

Our data showed that the use of povidone–iodine irrigation in the patients with DSWI has not led to any significant alteration in thyroid function within the study period.
References