Oral Triiodothyronine Normalizes Triiodothyronine Levels After Surgery for Pediatric Congenital Heart Disease

Eva M. Marwali, MD[1]; Cindy E. Boom, MD, PhD[1]; Indriwanto Sakidjan, MD, PhD[2]; Anwar Santoso, MD, PhD[2]; Dicky Fakhri, MD[3]; Ay Kartini, MD[4]; Aria Kekalih, MD[5]; Steven M. Schwartz, MD[6]; Nikolaus A. Haas, MD, PhD[7]

Objectives: This study was conducted to determine if oral triiodothyronine supplementation could prevent the decrease of serum triiodothyronine levels that commonly occurs after cardiopulmonary bypass for pediatric congenital heart surgery. Secondary objectives included identifying any significant adverse effects of oral triiodothyronine supplementation, including any effects on the thyroid/pituitary axis.

Design: Randomized, placebo-controlled, doubleblind clinical trial.

Setting: Operating room and ICU.

Subjects: Infants and children younger than 2 years of age undergoing congenital heart surgery using cardiopulmonary bypass (n = 43).

Interventions: Subjects were assigned to placebo (n = 15, group A) or one of two treatment groups: a low-dose group (group B, n = 14, 0.5 mcg/kg triiodothyronine orally every 24 hr for 3 d) or a high-dose group (group C, n = 14, 0.5 mcg/kg triiodothyronine orally every 12 hr for 3 d).

Measurements and Main Results: Thyroid hormone, including total and free triiodothyronine levels at predetermined time points, potential side effects indicatinghyperthyroidism, indicators of the thyroid-pituitary axis, and clinicalendpoints. Oral triiodothyronine supplementation twice-daily maintainedserum triiodothyronine levels within normal limits in groupC, whereas serum levels progressively declined in groups A and B. A statistically significant difference in triiodothyronine levels between the treatment groups occurred between 18 and 36 hourspost cross-clamp release, with the largest difference in serum levelsbetween group C and group A noted at 36 hours post cross-clamprelease (total triiodothyronine, 0.71 ± 0.15 [0.34–1.08] ng/mL [$p < 0.01$]; free triiodothyronine, 2.56 ± 0.49 [1.33–3.79] pg/mL [$p < 0.01$]). There was no evidence of hyperthyroidism or suppressionof the pituitary-thyroid axis in either treatment group.

Conclusions: Oral triiodothyronine supplementation at a dose of 0.5 mcg/kg every 12 hours for 3 days can maintain total and free triiodothyronine levels within normal limits after open-heart surgery using cardiopulmonary bypass for congenitalheart disease. (*Pediatr Crit Care Med* 2013; 14:00–00)

Key Words: cardiopulmonary bypass; congenital heart surgery; thyroid hormones

Cardiopulmonary bypass (CPB) in children is associated with a marked decline in thyroid hormone levels consistent with the phenomenon referred to as *sick euthyroid syndrome* (1). The decrease in thyroid hormone levels typically occurs between 12 and 48 hours after CPB, and these levels remain below normal for 5–7 days postoperatively (2). This transient decrease in thyroid hormone levels has been associated with increased morbidity, a greater use of inotropes and diuretics, as well as longer time on mechanical ventilatory support (3).

In infants and especially in neonates, a more profound reduction of triiodothyronine (T3), together with decreases in thyroxine (T4) and thyroid-stimulating hormone (TSH), is often detected. This scenario, described as sick euthyroid

[1]Department of Pediatric Cardiac Intensive Care and Anaesthesiology, National Cardiovascular Center Harapan Kita, Jakarta, Indonesia.

[2]Department of Cardiology and Vascular Medicine, National Cardiovascular Center Harapan Kita, Jakarta, Indonesia.

[3]Department of Pediatric Cardiac Surgery, National Cardiovascular Center Harapan Kita, Jakarta, Indonesia.

[4]Department of Clinical Pathology, National Cardiovascular Center Harapan Kita, Jakarta, Indonesia.

[5]Division of Epidemiology and Biostatistics, Department of Community Medicine, University of Indonesia, Jakarta, Indonesia.

[6]Department of Critical Care Medicine, The Hospital for Sick Children, University of Toronto School of Medicine, Toronto, ON, Canada.

[7]Department of Congenital Heart Defects, Heart and Diabetes Centre, North Rhein-Westfalia, Bad Oeynhausen, Germany.

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For information regarding this article, E-mail: evamarwali@yahoo.com

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syndrome type 2, might be related to increased morbidity, perhaps more so in pediatric patients compared with adult patients (4), leading to the speculation that postoperative thyroid supplementation might be of greater benefit to infants and small children (5). The largest randomized clinical trial so far, that is, the Triiodothyronine for Infants and Children Undergoing CPB (TRICC) study supported this hypothesis. Although TRICC found no benefit to the cohort as a whole, subgroup analysis showed a significant reduction in time to extubation, less use of inotropic support, and better cardiac function with T3 supplementation in patients under 5 months (6) and an increase in time to extubation in those older than 5 months. This finding is consistent with the notion that younger patients with complex operations and long bypass times might benefit most from T3 supplementation (7).

All previously published studies of T3 in this patient population have focused on the use of IV T3. This drug preparation, however, is not commonly used in many countries due to the relatively high costs and/or the simple lack of availability. The use of oral T3 to treat postoperative low T3 levels in pediatric patients has not been reported so far. Recent studies in adults demonstrated that postoperative serum T3 concentration was maintained in a more stable manner by oral T3 supplementation compared to the IV form (8, 9). These studies also suggested that oral T3 administration reduced vasopressor use (9).

The purpose of this study was to determine if oral T3 supplementation could prevent the decline of serum T3 in children less than 2 years undergoing congenital heart surgery using CPB. We hypothesized that oral T3 would increase both free and total thyroid hormone levels. Secondary objectives were to assess evidence of hyperthyroidism or adverse alteration of the thyroid-pituitary axis and to examine clinical outcomes.

PATIENTS AND METHODS

Design

This was a single-center, prospective, double-blind, randomized placebo-controlled trial to evaluate the effect of oral T3 supplementation to prevent a decrease of free and total T3 after CPB in children less than 2 years. Subjects were randomized into three groups of equal size. Group A received placebo (saccharum lactis) by nasogastric tube starting on induction of anesthesia and then every 12 hours until 60 hours postanesthesia induction (six doses totally). Group B was the low-dose treatment arm and received 0.5 µg/kg oral T3 (max 10 µg) (Tetronine, Dalim Biotech, Seoul, Korea) starting on induction of anesthesia and then every 24 hours alternating with placebo, which was given 12 hours after the first dose of oral T3 and then every 24 hours until 60 hours postanesthesia induction (three doses oral T3 and three doses placebo). Group C was the high-dose treatment group and received 0.5 µg/kg oral T3 (max 10 µg) starting on induction of anesthesia and then every 12 hours until 60 hours postanesthesia (six doses oral T3). The different dosing regimens were selected because of uncertainty surrounding enteral absorption in the perioperative period.

The Research Ethics Board at the National Cardiovascular Center Harapan Kita approved this study and this trial is registered with ClinicalTrials.gov (NCT01780584). Written, informed consent was obtained from the parents or legal guardians before randomization. Randomization by block permutation was performed to determine treatment group assignment. Randomization occurred on the day before surgery by a nurse investigator. A pharmacist who was not involved in the study prepared the study medication. Investigators and participants were blinded to the assigned group until after the end of the study.

Patient Characteristics and Conduct of CPB

Inclusion criteria were patients between 0 and 2 years with an Aristotle complexity score (10) of 6 and above who underwent cardiac surgery using CPB and were cared for in the Pediatric Cardiac Intensive Care Unit at the National Cardiovascular Center Harapan Kita, Jakarta, Indonesia between April 2010 and September 2010. Exclusion criteria were a birth weight less than 2 kg for neonates, preoperative tachyarrhythmia or need for antiarrhythmic treatment, clinical sepsis confirmed by culture, preoperative renal insufficiency (defined as serum creatinine > 2 mg/dL), known thyroid or metabolic disorder, or any contraindication for oral T3 administration. All CPB was nonpulsatile, and methylprednisolone 35–50 mg/kg was given to all subjects before CPB. Povidone-iodine was used for skin disinfection.

Measured Variables

The primary outcome was total T3 (TT3) and free T3 (FT3) levels during the first 72 hours after cross-clamp removal. Additional hormonal outcomes were total thyroxine (TT4) levels, free T4 (FT4) levels, and TSH levels. Hormonal levels were analyzed by standard third-generation TSH, FT4, FT3, and TT3 Microparticle Enzyme Immunoassays (Abbott Laboratories, Abbott Park, IL). The TT4 assay used a Fluorescence Polarization Immunoassay (Abbott Laboratories, Abbott Park, IL). Hormone levels were measured on induction of anesthesia, before the study drug was given (T0), and at 1, 6, 18, 36, and 72 hours after removal of the aortic cross-clamp.

Secondary outcomes assessed possible side effects of thyroid hormone supplementation, particularly those suggesting hyperthyroid symptoms within 7 days after surgery. Specific symptoms included cardiac dysrhythmia requiring medical or electrical treatment, hypertension (mean systolic or diastolic blood pressure more than two SDs above normal for age), and hyperthermia (> 37.5°C). Overt symptoms of hyperthyroidism were grounds for immediate removal of the subject from the study.

Baseline clinical data collected included age, gender, birth weight, type of operation, and Aristotle score. Diagnosis and operative procedures were classified as high or low risk with an Aristotle score cutoff of greater than or equal to 9 as high risk. Although this study was not powered to detect clinical differences between the treatment groups, clinical outcome variables were measured as a potential guide to subsequent

adequately powered larger treatment studies. Serum lactate was measured at 1 hour, 4 hours, and day 1 postsurgery. Hemodynamic monitoring included heart rate, heart rhythm, and blood pressure, which were recorded hourly for the first 6 hours and then every 6 hours until 72 hours after surgery. Time to extubation and length of stay in the ICU and hospital were recorded.

Statistical Analysis and Sample Size

The primary efficacy analysis assessed the difference between the treatment (high-dose, low-dose) and control groups with regard to the effect of T3 supplementation on the measured TT3 and FT3 serum levels. We anticipated a difference of 2.0 pg/mL in FT3 with an SD of 0.8 pg/mL between groups. For a statistical power of 80% to identify a treatment effect and at a level of significance of 0.05 (two sided), the target total sample size was 45 subjects, with 15 in each treatment group. Demographic data, safety, and clinical outcomes were compared using the chi-square test. Continuous variables for characteristics and outcomes were analyzed using one-way analysis of variance (ANOVA) for data with normal distribution or the Kruskal-Wallis test for not normally distributed data. Repeated-measures ANOVA was used to analyze all thyroid hormone levels and clinical outcomes for those variables that were measured repeatedly over time. Paired Student *t* test for parametric or Wilcoxon signed rank test for nonparametric tests were used to evaluate the mean difference of hormone levels and clinical outcomes over time in each treatment group. All calculations were done using SPSS 19 software (IBM, Armonk, NY). Statistical significance was defined by *p* values of less than 0.05. Descriptive statistics are reported as mean ± SEM.

RESULTS

Subject Allocation

There were 47 individuals screened for participation (**Fig. 1**), and consent to participate was obtained from 46 (98%). One subject from whom consent was obtained did not participate because of surgical postponement. A total of 45 subjects were randomized to three groups of 15. Two subjects (one in group B and one in group C) were withdrawn from the treatment protocol. The withdrawal in group B was because of severe hypertension caused by a previously unrecognized coarctation of the aorta, and the group C withdrawal was due to massive gastrointestinal bleeding that precluded the administration of oral T3. Therefore, there were 43 subjects included in the final analysis, with 15 subjects in group A and 14 subjects in each of groups B and C.

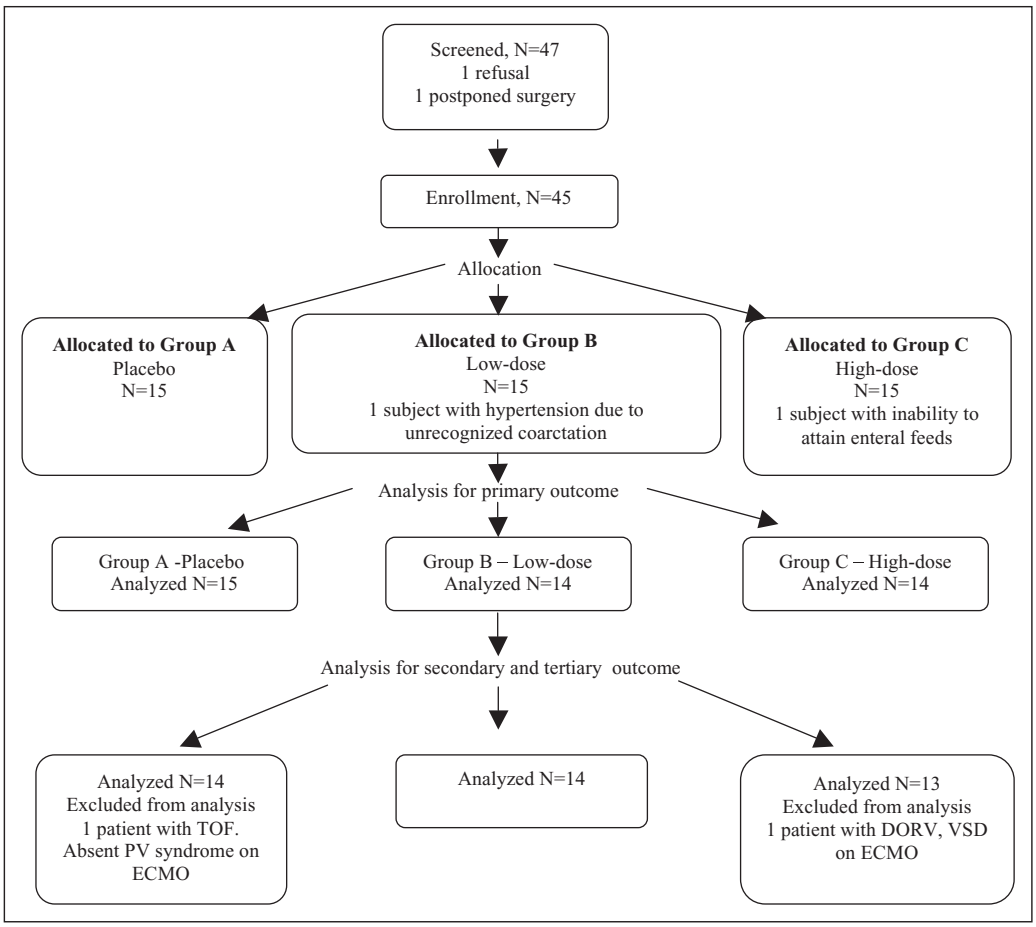

Figure 1. Flow diagram demonstrating subject recruitment, treatment group allocation, and those included in the outcome analysis. TOF = tetralogy of Fallot, PV = pulmonary valve, ECMO = extracorporeal membrane oxygenation, DORV = double outlet right ventricle, VSD = ventricular septal defect.

Subject Characteristics

The baseline and surgical descriptions of the subjects in each group are shown in **Table 1**. The three groups were similar in age, sex, birth weight, body weight at the time of surgery, and height. The mean age was 8.9 ± 0.67 months with a range of 0.5–24 months. The majority (76.7%) of subjects were older than 6 months. Most subjects (79%) were in the low-risk category (Aristotle ≥ 6 and < 9). The duration of surgery, defined as the time from induction of anesthesia to the release of the aortic cross-clamp, was 158.8 ± 5.8 minutes with a range of 110–280 minutes with no differences between the three study groups. There were also no differences between the groups in CPB time, cross-clamp time, the use

TABLE 1. Baseline Demographics and Surgical Data

	Group A $n = 15$	Group B $n = 14$	Group C $n = 14$	p
Age (mo)	9.7 ± 1.4	10.9 ± 1.6	10.9 ± 1.6	0.84
< 6 mo	3 (20.0%)	3 (21.4%)	4 (28.6%)	0.85
Male	5 (33.3%)	9 (64.3%)	6 (42.9%)	0.24
Birth weight (kg)	2.9 ± 0.1	2.9 ± 0.2	2.9 ± 0.2	0.87
Actual weight (kg)	6.5 ± 0.5	6.6 ± 0.5	6.0 ± 0.5	0.64
Height (cm)	67.3 ± 1.7	68.2 ± 2.1	66.9 ± 2.4	0.90
Type of surgery				
Ventricular septal defect closure	5 (30.0%)	5 (35.5%)	8 (57.1%)	
Tetralogy of Fallot repair	7 (46.7%)	4 (28.4%)	4 (28.6%)	
Incomplete atrioventricular canal repair	0	1 (7.1%)	0	
Arterial switch operation	1 (6.7%)	1 (7.1%)	1 (7.1%)	
Total anomalous pulmonary venous drainage repair	1 (6.7%)	0	0	
Absent pulmonary valve syndrome repair	1 (6.7%)	0	0	
Pulmonary atresia with ventricular septal defect repair	0	1 (7.1%)	0	
Double outlet right ventricle repair	0	0	1 (7.1%)	
Complete atrioventricular canal defect repair	0	2 (14.2%)	0	
Time of surgery (min)	154.8 ± 10.6	161.3 ± 9.0	160.6 ± 11.3	0.65
CPB time (min)	112.0 ± 15.7	131.1 ± 23.2	101.0 ± 16.9	0.57
Aortic cross-clamp time (min)	62.0 ± 6.4	66.3 ± 9.1	56.9 ± 8.2	0.56
Modified ultrafiltration	12 (80.0%)	12 (85.7%)	12 (92.3%)	0.56
Lowest CPB temperature (°C)	31.0 ± 0.5	31.5 ± 0.4	32.0 ± 0.4	0.31

CPB = cardiopulmonary bypass.
Variables are described with mean ± SEM or count (%).

of modified ultrafiltration, and the lowest temperature during CPB. None of the subjects received amiodarone during the study period.

Baseline Thyroid Hormone Levels (TT3, FT3, T4, FT4, and TSH)

Hormone levels were measured six times in each of the 43 study patients as per protocol. Two samples were unable to be analyzed (0.78%) due to missing blood samples; therefore, there were a total of 256 samples tested for each hormone. Results of hormone testing and reference values (11) for our laboratory are shown in **Table 2**. There was no baseline difference in TT3, FT3, T4, FT4, and TSH levels between the study groups. There were six subjects (14%) with low TT3 (< 0.8 ng/mL) levels at baseline, but this was not associated with increased TSH levels.

TT3 and FT3 Levels (Primary Outcome)

Serum FT3 and TT3 levels showed a continuous decline in both group A (placebo) and group B (low-dose oral T3) falling below the lower limit of normal by 18–36 hours post cross-clamp removal with minimal recovery by 72 hours. Group C (high-dose oral T3) maintained serum TT3 and FT3 levels above the lower limit of normal for the entire study period, although there was a reversion to levels similar to groups A and B by 72 hours, which was 12 hours after the final dose of study drug (**Fig. 2**). Repeated-measures ANOVA showed that the TT3 and FT3 levels at 18 and 36 hours post cross-clamp removal were significantly higher in group C compared to group A ($p = 0.022$ for TT3 and 0.025 for FT3) and not different from baseline. At 36 hours, 93.3% of subjects in group A and 71.4% in group B had TT3 levels lower than normal. In contrast, at the same time point, only four of 14 (28.6%) in group C had low TT3 levels ($p < 0.001$). FT3 showed the same pattern as TT3.

FT4, TT4, and TSH

All groups showed a decline of FT4, TT4, and TSH from time 0 through 72 hours after cross-clamp removal, although most of the TT4 and TSH levels remained above the lower limit of normal (11). Repeated-measures ANOVA found no differences between groups (Fig. 2).

TABLE 2. Baseline Thyroid Hormone Levels

	Group A *n* =15	Group B *n* = 14	Group C *n* = 14	*p* (A vs C)
TSH (μU/mL)	2.10 ± 0.39	3.51 ± 0.61	3.13 ± 0.42	0.36
TSH minimum-maximum	0.28–6.12	0.67–8.95	0.89–5.79	
nl: 0.4–11				
TT4 (μg/dL)	7.40 ± 0.35	7.40 ± 0.35	7.50 ± 0.47	1.00
TT4 minimum-maximum	5.23–9.64	5.23–9.64	5.23–9.64	
nl: 4.3–18.7				
FT4 (ng/dL)	1.16 ± 0.06	1.31 ± 0.06	1.19 ± 0.09	1.00
FT4 minimum-maximum	0.77–1.70	0.84–1.62	0.78–1.78	
nl: 0.9–3				
TT3 (ng/mL)	1.11 ± 0.10	1.16 ± 0.10	1.13 ± 0.10	1.00
TT3 minimum-maximum	0.51–1.66	0.36–1.81	0.49–1.96	
nl: 0.8–4				
FT3 (pg/mL)	3.69 ± 0.40	4.56 ± 0.60	3.71 ± 0.25	1.00
FT3 minimum-maximum	0.95–5.63	1.56–11.42	1.71–5.22	
nl: 2.5–10				

TSH = thyroid-stimulating hormone, nl = normal range for our laboratory, TT4 = total thyroxine, FT4 = free thyroxine, TT3 = total triiodothyronine, FT3 = free triiodothyronine.
Variables are described with mean ± SEM or range.

Undesired Hemodynamic Effects

There were no significant undesired hemodynamic effects noted in either of the treatment groups (B and C). Repeated measurements of heart rate, blood pressure, and temperature showed no significant difference among the three study groups (**Table 3**).

Clinical Outcomes

There were three deaths among the 43 subjects enrolled in the study. Two subjects who died, one each in groups A and C, were placed on extracorporeal membrane oxygenation in the operating room and are excluded from the following clinical outcome analyses. No significant differences were found in intubation time and length of stay in the ICU and hospital between groups (**Table 4**), although group B had the longest length of stay, primarily attributable to two subjects in group B with trisomy 21 undergoing repair of complete atrioventricular canal defects, in whom severe pulmonary hypertension, sepsis, and lung infection developed postoperatively. Another subject in group B, the third subject who died, had residual severe aortic insufficiency and complete heart block requiring placement of a permanent pacemaker after a 34-day ICU stay. Repeated-measures ANOVA of serum lactate at 1 hour, 4 hours, and 1 day postsurgery demonstrated a significant difference between group A and group C at 4 hours post-ICU admission, with mean difference of 0.81 mmol/L (p = 0.03). Mean serum lactate (95% CI) at 4 hours postsurgery was 3.2 (2.7–3.8) for group A, whereas it was 2.4 (1.9–2.9) mmol/L for group C.

DISCUSSION

To our knowledge, this is the first study of oral T3 supplementation in children to ameliorate the well-known and potentially clinically important decline in T3 that occurs after cardiac surgery. We demonstrated that oral T3, when given as 0.5 μg/kg (max 10 μg) starting on induction of anesthesia and then every 12 hours afterward, was effective in preventing this decline in T3. Furthermore, we did not detect any adverse effects, such as an increase in heart rate, blood pressure, or temperature, to suggest toxicity in this admittedly small cohort.

As demonstrated consistently in many other studies (2–4, 6), our study shows that T3 levels decrease after cardiac surgery. Studies in adults using oral T3 for supplementation in cardiac surgery patients have shown that oral T3 can prevent the decrease of TT3 and suggested hemodynamic benefits. Sirlak et al (8) treated patients with low ejection fraction undergoing coronary artery bypass grafting with oral T3 before and after surgery. Similar to the current study, they found that oral supplementation prevented the expected decline in thyroid hormone levels; they also found an improvement in left ventricular ejection fraction and a reduced use of inotropic drugs in the treatment group. Because of the number of subjects with complicated postoperative courses in group B as detailed above, we have chosen not to report differences in clinical outcomes, such as inotrope score or ventricular function, since any differences are unlikely to be primarily attributable to thyroid function. The emphasis in this relatively small trial was on the ability to normalize thyroid hormone levels rather than

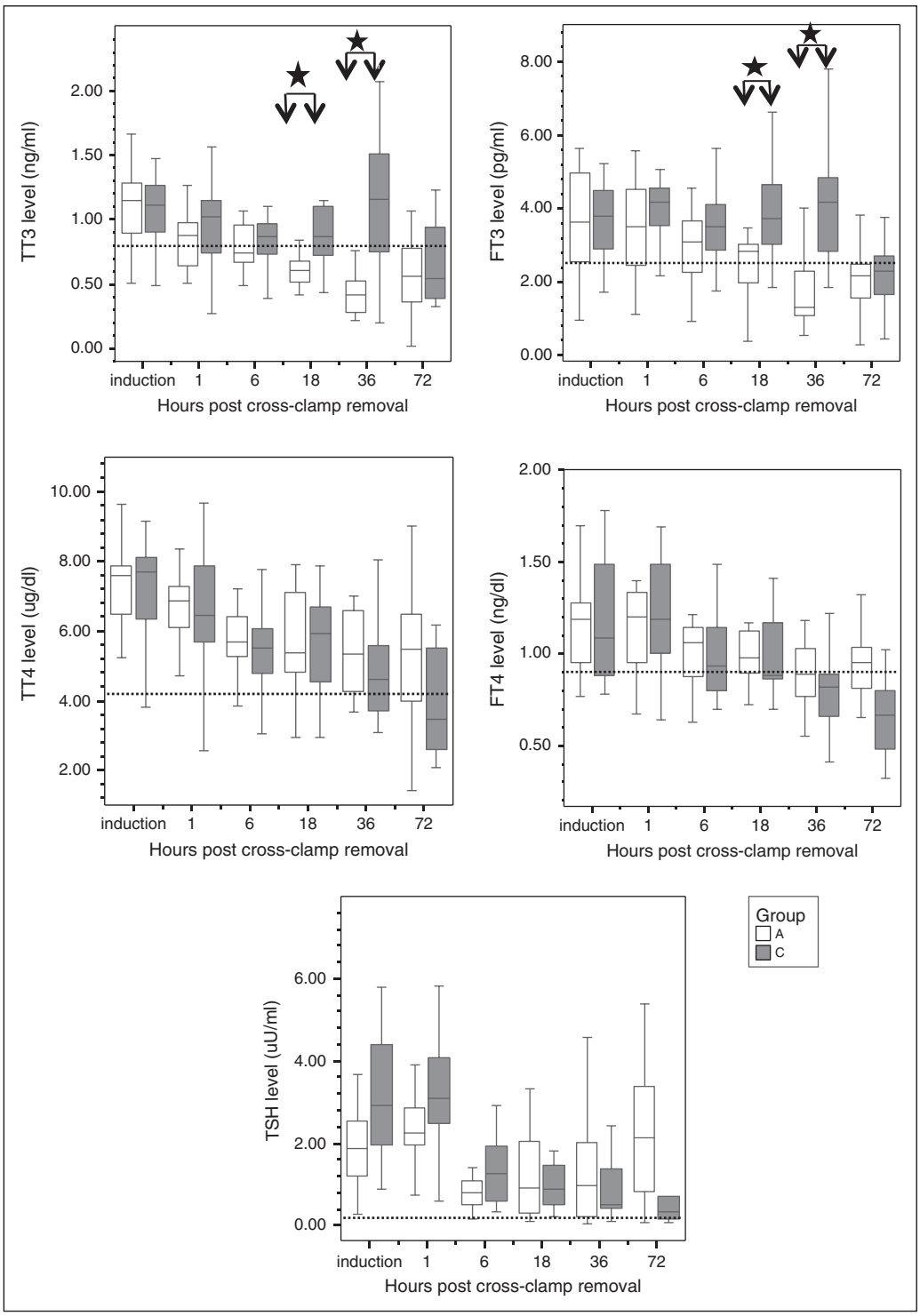

Figure 2. Thyroid hormone levels in group A and group C (group B was not different from group A and has been eliminated for clarity). Data are shown as median and 95% CI. Significant differences (*$p < 0.05$) were present between placebo and high dose at 18 and 36 hr post cross-clamp release. *Dotted line* indicates lowest normal limit for each measurement. TT3 = total triiodothyronine, FT3 = free triiodothyronine, TT4 = total thyroxine, FT4 = free thyroxine, TSH = thyroid-stimulating hormone.

clinical outcomes. Certainly these types of measurements will be important in a larger trial powered to clinical endpoints.

Mechanisms leading to low T3 levels in this population include the decline of iodothyronine deiodinase D2 activity, which is responsible for the conversion of T4 to T3, and an increase in iodothyronine deiodinase D3 activity, which promotes conversion of T4 to reverse T3, which is biologically inactive (12). Additionally, there is an inhibition in the central hypothalamic-pituitary axis, which results in a decrease in TSH together with T3 and T4 (13). In this study, TT3, FT3, TT4, FT4, and TSH all decreased after surgery in the placebo and low-dose oral T3 groups. It would appear then that the mechanism of the decreased T3 in this study is likely to be both peripheral and central inhibition in the hypothalamic-pituitary axis. This entity is described as low T3 syndrome, sick euthyroid syndrome type 2, and has primarily been described in small children (1).

Oral T3 supplementation is less expensive than the IV route. Oral T3 costs \$1.5–\$2 for a 25 mcg tablet compared to \$575 for a 1 mL vial containing 10 mcg IV solution. Furthermore, there may be clinical benefit because oral supplementation is not accompanied by the rapid increase of peak serum levels that have been reported after IV bolus administration (9). Specifically, IV bolus administration directly after cross-clamp has been associated with an increase of T3 levels to more than 3 ng/mL at 1 hour post cross-clamp release, although without remarkable side effects (6), whereas oral T3 maintained T3 levels in a stable manner similar to the data that we report. In the current study, oral T3 supplementation stably maintained TT3 and FT3 within the normal range in most patients in the high-dose group, with the highest levels noted at 36 hours post cross-clamp removal, and notably the peak T3 levels did not increase above highest normal limits. As the duration of surgery was 1.8–4.7 hours,

TABLE 3. Repeated-Measures Analysis of Variance

			p Post Hoc Test		
	F	*p*[a]	Group A Versus B	Group A Versus C	Group B Versus C
Mean arterial pressure	0.519	0.918	0.557	1.000	0.909
Systolic pressure	0.604	0.887	0.886	1.000	1.000
Diastolic pressure	0.751	0.702	0.347	1.000	0.839
Heart rate	0.943	0.566	1.000	1.000	0.726
Rectal temperature	1.093	0.370	0.545	0.096	1.000

[a]*p* value for (*F*) using Greenhouse-Geisser test.

TABLE 4. Clinical Outcomes by Treatment Group

	Group A (*n* = 14)	Group B (*n* = 14)	Group C (*n* = 13)	*p*
Intubation time (hr)	23 (15–144)	36.5 (5–794)	17 (8–224)	0.31
Length of stay in ICU (hr)	48.5 (20–258)	109.5 (22–816)	87 (22–456)	0.40
Hospital length of stay (d)	6 (5–26)	17.5 (2–34)	10 (5–41)	0.06

Data are presented as median (min-max).

presumably the peak serum levels were reached at 37.8–40.7 hours after initial drug administration. These serum levels are compatible with the known pharmacokinetics of this drug that reaches peak levels by 24 hours and has a half-life of 2 days in euthyroid subjects (14).

This study did not show any differences in mechanical ventilation time or length of hospital or ICU stay associated with the repletion of thyroid hormone levels. Although a longer length of intubation and hospital stay were noted in low-dose group, this was associated with specific surgical issues and complications and is not attributable to the study treatment. Given that the majority of subjects in this study underwent primary closure of a ventricular septal defect and that this operation is not usually associated with a prolonged or complicated postoperative course, it is not surprising that clinical considerations outweigh hormonal replacement in dictating clinical outcomes in this cohort. Nevertheless, when considered together with other studies that have demonstrated some evidence of hemodynamic benefit associated with normalization of thyroid hormone levels (6, 15), there is compelling data to support a trial of oral T3 supplementation in subgroup of infants less than 5 months, powered appropriately for clinically important endpoints. Despite the relatively small study group, serum lactate was significantly lower at 4 hours after surgery in the high-dose treatment group compared to the placebo group. Lower lactate levels may indicate a more effective metabolism and/or better tissue perfusion. Given the differences in morbidity attributable to the underlying disease accounting for differences in length of stay outcomes, it seems unwise to place too much importance on this finding.

The primary limitations of this study relate to the lack of power to detect differences in clinical outcomes as discussed above. An important consideration in comparing our study to the TRICC trial is that most of the subjects in the current study were over 6 months old, whereas the primary benefit in TRICC was to infants less than 5 months. A larger clinical trial of oral T3 supplementation might need to be focused on those younger than 5 months. There was also insufficient power to detect potentially subtle adverse effects of T3 supplementation. There was, however, no indication of any clinically important trends in blood pressure, heart rate arrhythmias, or temperature to suggest toxicity. Furthermore, we only observed subjects for possible clinical adverse effects until 7 days after surgery. We did not see any suppression of TSH in three groups at the end of our study. Given that effects of thyroid supplementation on the pituitary-thyroid axis could occur up to 120 hours post-supplementation as demonstrated in other studies (16), longer periods of observation on pituitary-thyroid axis are likely to be important in future studies. In the larger picture, the clinical significance of normalization of T3 levels remains uncertain. Furthermore, restoration of feedback loops involving TSH and thyrotropin-releasing hormone may have an important role in restoring the hypothalamic-pituitary-thyroid axis following cardiac surgery and similar stressors. Our study found no differences in TSH levels between treatment groups, suggesting that oral T3 is unlikely to affect these aspects of thyroid regulation.

CONCLUSION

Oral T3 supplementation at a dose of 0.5 mcg/kg every 12 hours for 60 hours was able to maintain normal TT3 and FT3 in children less than 2 years undergoing open-heart surgery without any evidence of significant adverse effects. Further research is warranted to evaluate the potential for oral T3 supplementation to improve clinical outcomes in this population.

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