Congenital Heart Disease

Euthyroid Sick Syndrome after Open Heart Surgery

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Background: The hemodynamic effects of thyroid hormones are well documented, and include effects on cardiac contractility, heart rate and myocardial oxygen consumption.[1] Major cardiac surgery under cardiopulmonary bypass (CPB) support may produce many alterations in endocrine homeostasis, which can exert substantial hemodynamic effects postoperatively.[2] Twenty patients with various congenital heart diseases (CHDs) were enrolled to analyze their thyroid function before, during and after cardiac surgery.

Materials and Methods: We found that there were short-term reversible postoperative declines in free thyroxine (T4), total T4, total tri-iodothyronine (TT3) and thyrotropin concentrations. TT3 decreased significantly from preoperative state to 30 min after the start of CPB ($p = 0.007$) and 1 day postoperatively ($p = 0.008$). The significant changes of the thyroid hormones in our 20 patients belonged to the euthyroid sick syndrome (ESS). There was no surgical complication and no need for thyroid hormone replacement. All these patients recovered and were discharged home smoothly.

Conclusions: We conclude that patients with CHDs under cardiac surgery might present with ESS in postoperative period, but have no need for thyroid hormone replacement and will recover spontaneously within one week.

Key Words: Cardiac surgery • Cardiopulmonary bypass • Congenital heart disease • Euthyroid sick syndrome • Thyroid function

INTRODUCTION

It is well documented that thyroid function will be affected by severe systemic illnesses and major surgical procedures.[3-5] Open heart surgery supported by cardiopulmonary bypass (CPB) is a major stress on both psychologic and physiologic aspects. Previous studies of CPB on thyroid function are conflicting and inconclusive.[2-4,6-12] Thyroid function is usually depressed during and after cardiac surgical procedures, which can adversely affect the myocardial performance and even the outcomes of surgery. To evaluate and analyze the thyroid function before, during and after open heart surgery for congenital heart diseases (CHDs), twenty patients who underwent open heart surgery with CPB support were enrolled for study.

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MATERIALS AND METHODS

Study Patients

This study consisted of 20 patients with various CHDs who underwent open heart surgery with CPB support during the period of August 2002 to June 2003 at our institution. Patients who weighed less than 5 kg were

excluded because of the risk of excessive blood loss from frequent blood sampling.

Data Collection, Hormone Analysis and Statistical Analysis

After informed consents was obtained, the patients had their blood samples drawn for the determination of free thyroxine (T4), total T4 (TT4), total tri-iodothyronine (TT3) and thyrotropin (TSH) in the following periods: 1-2 days preoperatively, 30 min after the start of CPB, and 1, 2 and 7 days postoperatively. The measurements of thyroid hormones were performed by radioimmunoassay technique using Coat-A-Count® kits (D. P.C., Los Angeles, USA) for TT3 as well as TT4 detection, and RIA-gnost® kits (C.I.S. Bio International, Yvette Cedex, France) for free T4 and TSH detection. Normal values of free T4, TT4, TT3, and TSH were set 0.8-1.8 ng/dL, 5-12 ng/dL, 70-220 ng/dL, and 0.4-5.0 uU/mL, respectively.

All demographic, clinical and technical data were collected prospectively in standard forms, entered into a computer database and expressed as mean values (see Table 1). Results of the thyroid hormone measurements were presented as mean ± standard error of the mean (Figures 1-4). These data were analyzed by SPSS software (10.0). The changes of thyroid hormones between preoperative, perioperative and post-operative statuses were compared by one way ANOVA and Turkey's test. Significance was defined as p value < 0.05.

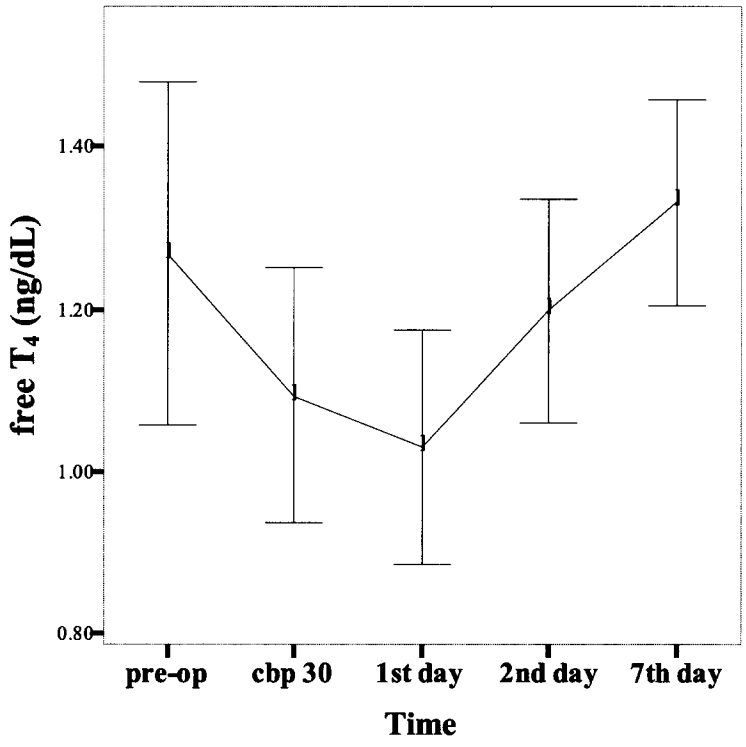
RESULTS

The patients' characteristics are shown in the Table 1. The study group consisted of 20 patients: 14 male (70%) and 6 female (30%) with a mean age of 8y3m (range, 10m to 33y10m). The mean values of body height and weight were 115.9 cm and 31.0 kg. The mean body surface area was 0.97 m^2. The mean duration of aortic clamping and CPB were 54.2 and 85.7 min, respectively. Fifteen patients underwent ventricular septal defect repairs, three for atrial septal defect repairs, one

Table 1. Data for 20 patients

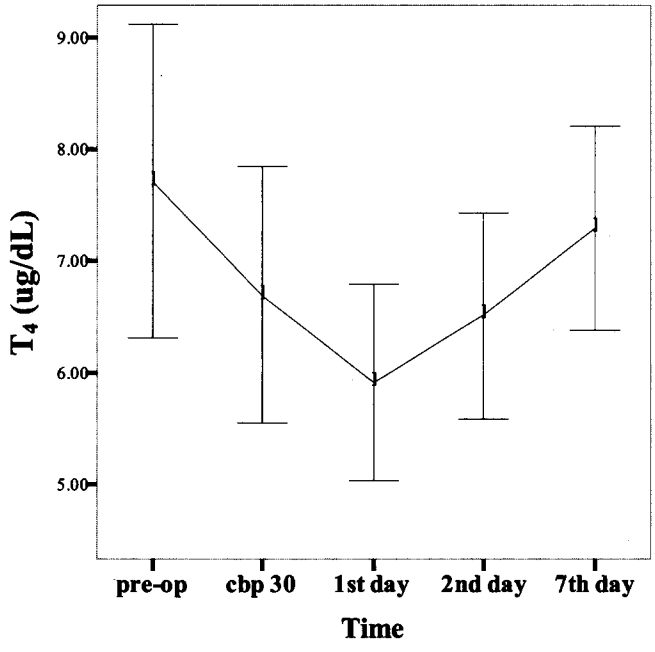
Patient No.	Sex	Age	Height (cm)	Weight (kg)	BSA (m^2)	Duration (min) of		Operative procedures
						AO clamping	CPB	
1	F	1y2m	72	9	0.42	35	57	VSD closure
2	F	1y1m	69	7	0.37	26	52	VSD closure
3	M	3y5m	94	11	0.54	37	63	ASD closure
4	F	22y6m	160	58	1.61	35	80	VSD closure
5	M	1y3m	72.5	10	0.45	26	80	VSD closure
6	M	6y7m	130	32	1.07	44	70	VSD closure
7	M	2y1m	91	15.5	0.63	36	53	VSD closure
8	M	6y3m	138	32.5	1.12	33	61	VSD closure
9	M	6y8m	115	23	0.85	35	48	ASD closure
10	F	6y5m	154	70	1.73	47	70	VSD closure
11	M	1y7m	82	10.9	0.5	28	51	VSD closure
12	M	10m	68	7.2	0.37	55	74	VSD closure
13	F	33y10m	155	56	1.55	59	100	VSD closure
14	F	22y0m	152	44.5	1.37	52	71	VSD closure
15	M	1y11m	73	9.1	0.43	167	259	Arterial switching operation
16	M	21y0m	160.5	73	1.8	136	160	Aortic valve replacement
17	M	9y7m	128.5	27	0.98	31	76	VSD closure
18	M	8y11m	175	67.5	1.81	83	111	ASD closure
19	M	12y3m	155	49	1.45	47	77	VSD closure
20	M	1y9m	74	8.5	0.42	72	100	VSD closure
Mean		8y3m	115.9	31.0	0.97	54.2	85.7	

Abbreviations: AO = aorta; ASD = atrial septal defect; BSA = body surface area; CPB = cardiopulmonary bypass; F = female; M = male; VSD = ventricular septal defect.



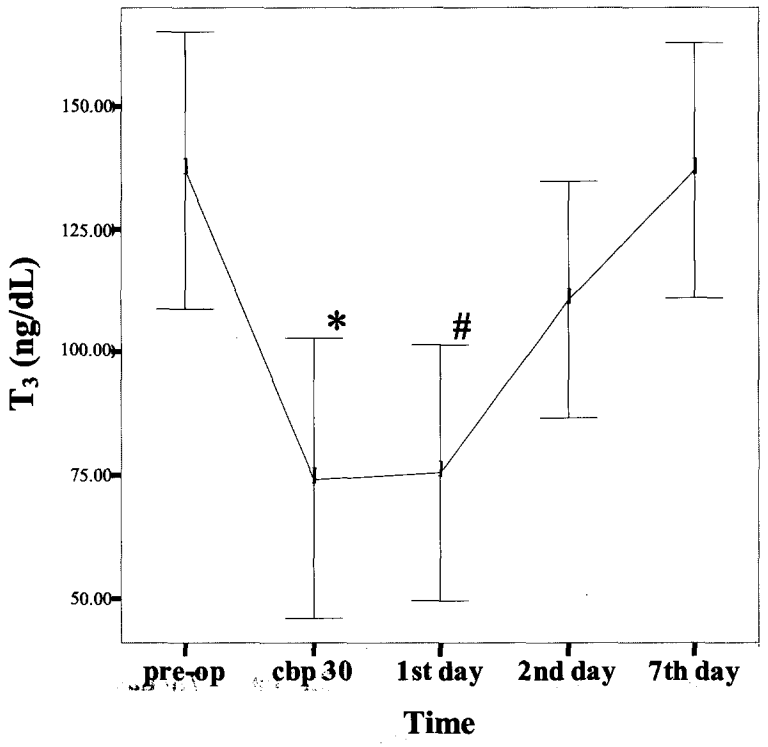
Normal values are as follows: 0.8-1.8 ng/dL.
Abbreviations: pre-op: pre-operation; cbp 30: 30 min after the start of cardiopulmonary bypass; 1st, 2nd, and 7th day: first, second, and seventh day after surgery.

Figure 1. Perioperative changes in free T_4 concentrations. Vertical bars represent mean ± standard error of the mean.



Normal values are as follows: 5-12 ng/dL. Time abbreviations are the same as in Figure 1.

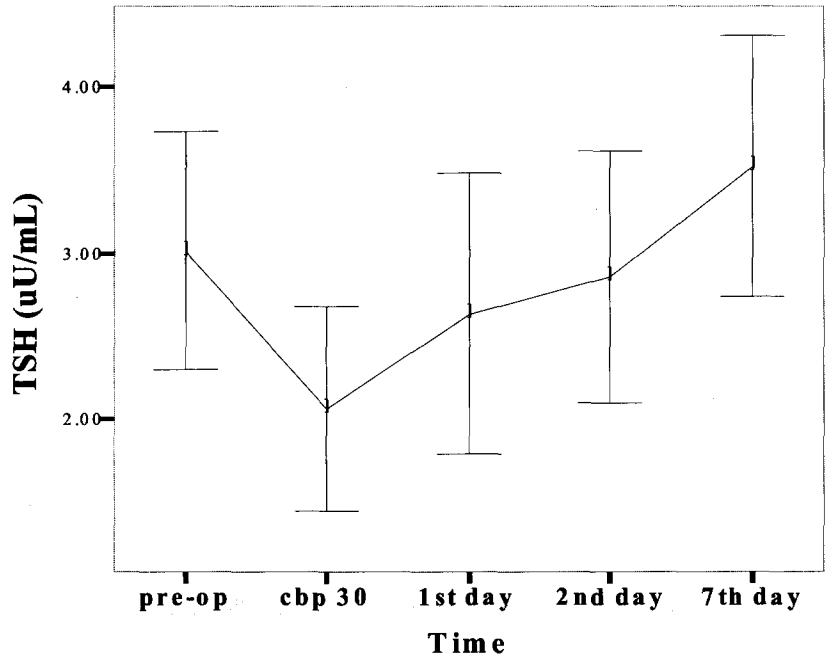
Figure 2. Perioperative changes in total T_4 concentrations. Vertical bars represent mean ± standard error of the mean.



*: $p = 0.007$; #: $p = 0.008$

Normal values are as follows: 70-220 ng/dL. Time abbreviations are the same as in Figure 1.

Figure 3. Perioperative changes in total T_3 concentrations. Vertical bars represent mean ± standard error of the mean.



Normal values are as follows: 0.4-5.0 uU/mL. Time abbreviations are the same as in Figure 1.

Figure 4. Perioperative changes in TSH concentrations. Vertical bars represent mean ± standard error of the mean.

for arterial switching operation, and one for aortic valve replacement. The values of free T4, TT4, TT3, and TSH are summarized in Figures 1-4. TT3 levels decreased in 16 patients and with statistical significance from preoperative state to 30 min after the start of CPB ($p = 0.007$) and to 1 day postoperatively ($p = 0.008$). The changes of free T4, TT4 and TSH levels followed a pattern similar to that of TT3. TT3 and TSH reached minimum 30 min after the start of CPB. Free T4 and TT4 reached minimum in the first day after surgery. All patients had successful operations without complication.

DISCUSSION

The thyroid gland produces three different hormones: T4, T3 and reverse T3 (RT3). T3 is 3 to 5 times as potent as T4 and mainly produced by peripheral deiodination of T4 in the liver and kidney, and only 10-20% is produced by the thyroid gland. The peripheral deiodination of T4 is under strict hormonal and metabolic control.[3]

Compared with preoperative data, our results indicated that thyroid function, especially the level of TT3, depressed during and immediately after open heart surgery, which is consistent with the findings in ESS. Thyroid hormones in ESS are usually characterized by normal concentrations of free T4, TT4 and TSH, increased concentration of RT3, and decreased concentrations of free T3 and TT3;[6,13-15] whereas in primary hypothyroidism, decreased concentrations of free T4 and TT4, increased concentration of TSH, and normal concentrations of free T3 and TT3 are characteristically observed. ESS is usually observed as an acute alteration of the thyroid axis in response to many kinds of systemic illnesses (or stress).[3,7-9,16,17] Physical stress reduces the deiodination process of T4 to T3 and increases the synthesis of RT3 without any increase in the TSH level.[18] It has been suggested that the declines in the free thyroid hormone levels may in part be involved in the pathophysiologic mechanism of a low cardiac output state that may occur after operation. Fortunately, this syndrome will usually revert to normal without hormone supplement.

The mechanism postulated for ESS involves regulation of specific deiodinases in T4 metabolism.[6,19,20] Two deiodinases are involved in the stepwise deiodination of T4: 5′-deiodinase converts T4 to T3 and RT3 to 3,3′-T2, and 5-deiodinase converts T4 to RT3 and T3 to 3,3′-T2. It is postulated that diminished activity of 5′-deiodinase results in decreased formation of T3, thus allowing increased conversion of T4 to RT3 by 5-deiodinase. In addition, there is a concomitant diminished metabolism of RT3 to 3,3′-T2, which contributes to the large elevation of RT3.[3,6,19]

Thyroid hormone has also been considered a treatment for patients with congestive heart failure, for patients with hyperlipidemia, and for patients undergoing CPB and heart transplantation.[21] At present, there is no evidence to suggest a favorable treatment outcome using thyroid hormone supplement for any systemic condition, except in those patients with documented hypothyroidism. Administration of T3 to patients who manifest the ESS is still controversial.[10,22] Studies are limited, and optimal management is undetermined. Preoperative thyroid replacement in patients with coronary artery disease may precipitate acute myocardial ischemia or infarction.[3,23] Whether patients with ESS should be treated has yet to be resolved. This study found no adverse perioperative events, which indicates that immediate thyroid hormone replacement therapy may not be necessary for patients with ESS. Treatment of children with T3 after CPB could raise T3 plasma concentration and improve myocardial function, especially in patients with low postoperative cardiac output.[24]

Preoperative thyroid hormone replacement is needed in case of nonurgent operation for those patients with overt hypothyroidism and possibly those with mild hypothyroidism (i.e., normal T4 and elevated TSH levels, with symptoms attributable to thyroid underactivity).[11]

The limitation of the present study lies mainly in the following two specific issues. Firstly, although the transient decreases of thyroid hormones found in immediate post operation were statistically significant, yet the amount of decreases was still within normal limit and it may raise questions about the clinical implication of the present findings. Secondly, the decrease of T3 and T4 associated with the decrease of TSH has been suspected to be the effect of hemo-dilution seen post operatively. However, we did not see similar dilution in the complete blood count data of those patients, and

therefore, we can exclude the transient decrease of TSH seen in our patients with ESS were the result of hemodilution. We did not know the exact etiology for decrease of TSH.

In summary, our study support that open heart surgery under CPB can produce ESS in the perioperative period, and that ESS is transient with no adverse events. We also conclude that patients with CHDs undergoing cardiac surgery do not require routine thyroid function examination, and that ESS does not need thyroid hormone replacement therapy.

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開心手術後之正甲狀腺功能疾病症候群

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背景 甲狀腺素對於血液動力學上的影響已被相當地瞭解。它們對身體的影響包括：增強心臟收縮、加快心跳速率、以及增加心臟肌肉的氧氣消耗等等。先天性心臟病的病患，藉由心肺機器來輔助開心手術，也會造成身體許多內分泌的改變，進而造成手術後血液動力學上的影響。在此，我們總共納入了二十位先天性心臟病的患者，分別在手術前、中、後抽血，來分析他們甲狀腺功能變化的情形。

方法 我們發現甲狀腺功能在手術後有一短暫的下降情形；其中特別是三碘甲狀腺素 (tri-iodothyronine) 在心肺機開始三十分鐘、及手術後一天，皆有明顯地下降，並且達到統計學上有意義的變化。在此二十位病人的研究當中，甲狀腺功能的變化屬於正甲狀腺功能疾病症候群 (euthyroid sick syndrome)，並且手術並沒有併發症產生，也沒有任何一位病人有接受甲狀腺素的治療，所有的病人都順利的康復與出院。

結論 對於本篇的研究，我們認為患有先天性心臟病的病患，在接受開心手術之後，會出現短暫的正甲狀腺功能疾病症候群，但是這樣的甲狀腺功能變化，並不需要任何的甲狀腺素治療，而且正甲狀腺功能疾病症候群會在短時間 (約一週) 內自行恢復正常。

關鍵詞： 心臟手術、體外心肺循環機、先天性心藏臟病、正甲狀腺功能疾病症候群、甲狀腺功能。