

Subclinical hypothyroidism affects the intraoperative and postoperative hemodynamics in coronary artery bypass graft surgery: should we supplement with thyroxine preoperatively

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Background

Our aim was to reveal the effect of the subclinical hypothyroid state on cardiac surgery, to derive a conclusion to include thyroid profile tests as a routine in cardiac surgery patients, and to know the role of thyroxine supplementation preoperatively in subclinical hypothyroid patients on the perioperative course.

Patients and methods

Between March 2007 and April 2010, we operated upon 87 patients of coronary artery revascularization, who had subclinical hypothyroidism as confirmed by laboratory investigations [high thyroid-stimulating hormone (TSH) and normal levels of T3 and T4]. We divided them into two groups: group A included patients who received preoperative thyroxine (47 patients) and group B included patients who were not supplemented with thyroxine preoperatively (40 patients). Preoperative, intraoperative, 24-h postoperative, and before discharge assessment of the cardiac function [ejection fraction percent (EF%)] as well as assessment of the thyroid profile (TSH, T3, and T4) were performed in all patients in both groups.

Results

We found an increased incidence of operative and postoperative complications in group B than in group A. The intraoperative and immediate postoperative EF% showed significant myocardial depression in group B ($P < 0.003$) and group A ($P < 0.001$) when compared with preoperative value. After 24 h of operation, the effect of thyroxine started to appear with a marked improvement in the cardiac functions in both groups. In group B, the EF% improved from $37.5 \pm 3.07\%$ at 12 h after operation to $45.6 \pm 2.0\%$ at 24 h after operation and to $53.76 \pm 7.7\%$ just before hospital discharge. With respect to the thyroid profile, there was a marked decrease in the level of T3 in group B intraoperatively (0.9 ± 0.3 pg/ml; $P < 0.002$). The level was corrected 24 h postoperatively, after the intake of the Eltroxine, to 2.3 ± 0.8 pg/ml and then to 2.5 ± 1.1 pg/ml before hospital discharge. The level of TSH was markedly increased in group B intraoperatively (14.3 ± 4.7 μ IU/l; $P = 0.007$ between both groups). The TSH level started to decrease in both groups after intake of Eltroxine in hospital. There was an increased incidence of supraventricular arrhythmias, mainly atrial fibrillation (four cases in group A and eight cases in group B).

Conclusion

Thyroid function tests should be a routine preoperative investigation in any patient admitted for cardiac surgery. The preoperative supplementation of thyroxine is vital and decreases the operative and postoperative morbidity and mortality in patients with subclinical hypothyroidism.

Keywords:

coronary artery bypass graft surgery, subclinical hypothyroidism

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Introduction

Any person under stressful conditions may suffer from disturbed thyroid hormones, subclinical hypothyroidism (SCHT), or even frank hypothyroidism as confirmed by laboratory measurements [1]. The incidence of hypothyroidism and SCHT depends on many factors; the commonest are iodine deficiency and autoimmune thyroiditis. The first is more common in the Middle

East, increasing much more in the endemic areas all over the world. Of them is the gulf area, specifically the Saudi Arabia. Although some may regard its treatment unnecessary, others may look to this point cautiously with adjusted doses and strict follow-up because of fear of poor compliance of the patients or drug interactions and even sometimes overdose, which is common in clinical practice increasing the risk of atrial fibrillation (AF) and osteoporosis [2].

There is no debate on the treatment of hypothyroidism among physicians, but the question is to treat or not to treat the subclinical cases. The subclinical states may be treated with a daily single dose of thyroxine. This treatment requires monitoring of the thyroid hormones in the blood over several months. Although it is not certain whether the treatment of SCHT is necessary at all, the treatment is warranted, especially if the blood level of the thyroid-stimulating hormone (TSH) is above 10 mU/l [3]. Although the TSH range defining SCHT remains elusive, the upper limit of 10 mU/l, which has been quoted in the literatures, is not met in most patients of SCHT, as most of them (75%) have values less than this (average of 7 mU/l) [4].

SCHT has an incidence of 8–10% and may increase up to 20–30% after the age of 60 in female individuals. It may be also referred as infraclinical hypothyroidism, borderline hypothyroidism, biochemical hypothyroidism, or early-aged pituitary syndrome. Irrespective of the name, those patients might be unnoticed clinically, as they complain of general nonspecific symptoms: lethargy, easy fatigue, or constipation. The diagnosis is only on the basis of laboratory findings of high TSH and normal levels of T3 and T4 [5].

Thyroid hormones greatly affect the cardiovascular system even in the subclinical states, which might be unnoticed. SCHT may lead to impaired left ventricular diastolic function at rest, impaired systolic function on effort, enhanced risk for atherosclerosis and myocardial infarction (MI), increased left ventricular mass with marginal concentric remodeling, impaired ventricular relaxation, reduced exercise performance with an increased heart rate and high incidence of arrhythmias, and finally increased risk for cardiovascular death [6]. The benefits of treatment against the potential risks have been evaluated and weighed by many authors. It might be of value in symptomatic patients or those undergoing major surgeries, whereas it may be risky because of its side effects such as MI or its iatrogenic hyperthyroidism. Patients with AF or osteopenia may benefit from early treatment with thyroxine [7,8].

The effect of cardiopulmonary bypass (CPB) on the level of thyroid hormones was previously investigated, revealing that the TSH was initially increased during the bypass and then normalized on the first postoperative day. In addition, minor alterations in free T4 were observed. T3 and free T3 declined at the start of CPB and then T3 remained low during the whole postoperative period, whereas free T3 returned to normal on the first postoperative day [9]. Aslan *et al.* [10] recently discovered a method to regulate TSH and T3 in cardiac cases with CPB by administration of sodium

nitroprusside (through its release of nitric oxide) during CPB, which regulated the levels of T3 and TSH. Yet, this study has a good result without clear explanation. Some other authors performing their procedures off-pump had found the effect of cardiac surgery or even major surgeries on the level of the thyroid hormones, although it was discovered that CPB may cause this, such as aggravation of the already present hypothyroidism or even the SCHT to the frank state of hypothyroidism [11]. Although less invasive than the CPB, the off-pump coronary artery bypass graft surgery (CABG) also causes the nonthyroid illness syndrome, resulting in lack of conversion from T4 to T3. In addition, it leads to high TSH in euthyroid patients [11].

Irrespective of the cause, the fact is that we still have a question to be answered whether thyroxine be given to the asymptomatic patients of SCHT, admitted for cardiac operations (on-pump or off-pump), exposing them to the risk of arrhythmias and even MIs, or not be given, thus exposing them to a stormy operative and postoperative time, even mortality?

Materials and methods

Patient recruitment and study protocol

Between March 2007 and April 2010, we operated 87 patients known to have SCHT confirmed by laboratory investigations for CABG. After approval of the protocol by the institutional review board, written informed consent was obtained from all participants. This prospective, randomized, double-blind study was conducted in the cardiothoracic surgical unit in a tertiary hospital in Saudi Arabia. Nurses who did not participate in the study gave the medication to the patients according to the table of randomization. Drug administration and data collection were performed in a double-blind manner in which neither the patient nor the medical team was aware of the drugs.

All patients had ejection fraction (EF) more than 45%. The patients were randomized by sealed envelopes into two groups: group A (47 patients) received preoperative thyroxine and group B (40 patients) did not receive thyroxine preoperatively. All patients in group A received preoperative Eltroxine (GlaxoSmithKline) at a dose of 50 µg/day: two doses 48 h before surgery and a third dose on the day of surgery (50 µg). At the same time, patients in group B received placebo tablets — Domperidone 10 mg (stomach discomfort relief tablets) — in the same schedule such as Eltroxine. Patients in both groups received thyroxine (Eltroxine) supplementation 12 h postoperatively at a dose of 100 µg and then a maintenance dose of 50 µg/day, either orally or

through nasogastric tube if the patients had delayed recovery. Both groups were clinically assessed by history-taking and thorough clinical examination and were investigated preoperatively for complete blood count, coagulation profile (INR, PC, PT, and PTT), liver, kidney, and thyroid functions, echocardiography, carotid duplex, chest radiograph, and abdominopelvic ultrasonography. We excluded the following groups of patients from the study: unstable patients, patients with recent MI, recent or old strokes, significant carotid stenosis, renal impairment or failure, hypothyroidism (uncontrolled), controlled hypothyroidism, redo cardiac surgeries, cardiomyopathy, EF less than 45%, old aged (above 70 years old), recent thrombolytic therapy, minimal invasive procedure, awake CABG, and finally patients with SCHT taking thyroxine previously.

Anesthetic and surgical techniques

Patients received their usual cardiac medications early morning on the day of surgery. Premedication consisted of diazepam 5 mg and ranitidine 150 mg orally the night before surgery. On the day of surgery, morphine 0.1 mg/kg intramuscularly was given 2 h preoperatively. After arrival in the operating room, all patients were given intravenous midazolam 0.03–0.05 mg/kg. A five-lead ECG using continuous ST segment analysis, pulse oximetry, and noninvasive blood pressure monitoring was initiated. After performing modified Allen's test, an arterial catheter was inserted, under local anesthesia, into the radial artery for invasive blood pressure monitoring and arterial blood gases measurements. General anesthesia induction consisted of fentanyl 5–10 µg/kg, propofol 1 mg/kg, and cisatracurium 0.15 mg/kg. After the trachea was intubated, a right internal jugular multilumen central venous catheter was inserted. Anesthesia was maintained using isoflurane 0.5%, and its concentration was later adjusted as required by the clinical conditions (heart rate and blood pressure). Neuromuscular blockade was achieved by an infusion of cisatracurium at a rate of 3 µg/kg/min. Heparin sulfate 2 mg/kg was administered before distal separation of the left internal thoracic artery and then supplemented as needed to maintain an activated clotting time of at least 200 s. We used the routine epidural analgesia, but we failed insertion in nine patients (four in group A and five in group B). Epidural catheter was inserted on the day of surgery (after checking an early morning coagulation profile) at T4–T5 level using a midline approach. A test dose of lidocaine 2% was given followed by a bolus of 4–8 ml of bupivacaine 0.25% and fentanyl 50 µg 10–20 min before incision; thereafter, an infusion of bupivacaine 0.125% and fentanyl 2 µg/ml was started at a rate of 10 ml/h.

The midline skin incision was performed with median sternotomy. The procedure performed was off-pump CABG for all patients in both groups using the Medtronic Octopus version 4.3 (Medtronic Inc., Washington, DC, USA). The great saphenous vein was harvested in 45 patients in group A (95.7%) and in 39 patients in group B (95%). Left internal thoracic artery was harvested and anastomosed to LAD in all patients in both groups. The radial artery was harvested in 37 patients in group A (78.7%) and in 28 patients in group B (70%). Posterior pericardiotomy at the end of the procedure was performed in all cases, with two tubes introduced through the anterior mediastinum by two separate stabs at the lower end of the midline incision. The left tube directed to the left pleura and the other to the anterior mediastinum. No bilateral mammaries or Y and T anastomoses were performed. After the proximal anastomosis, heparin activity was neutralized with protamine sulfate at the end of the surgery and then all patients were transferred to the ICU.

Myocardial systolic function assessment

Preoperative assessment of systolic function (EF%) was performed using transthoracic echocardiography (TTE) as a part of routine investigations. Intraoperative assessment was performed by transesophageal echocardiography (TEE) in all patients in both groups. The probe was inserted after the induction of anesthesia and kept until just before transfer to the ICU. The cardiac function was assessed after revascularization, and the data were recorded. TTE was performed again in all patients in both groups at 12 and 24 h after surgery and before hospital discharge.

Blood sampling and biochemical assays

T3, T4, and TSH were measured preoperatively, intraoperatively at the end of the procedure, after 24 h, and finally before hospital discharge. Measurements were taken using fasting serum samples collected from all patients and processed within 30 min using the Architect System machines. The kits were obtained from Architect System Company. We assayed the levels of T3 and free T4 using the Architect ci 4100.

T3 assay

Architect free T3 assay is a chemiluminescent microparticle immunoassay (CIMA) for the quantitative determination of free T3 in human serum and plasma. The reagent kit used is 7K63. The default result is expressed in pg/ml ($\times 1.536 = \text{conc. in pmol/l}$) with a normal range of 1.71–3.61 pg/ml, and the analytical sensitivity is less than 1.0 pg/ml.

T4 assay

Architect free T4 assay is a CIMA for the determination of free T4 in human serum and plasma. The reagent kit used is 7K65. The default result is expressed in ng/dl ($\times 12.87 = \text{conc. in nmol/l}$). The normal range is 0.70–1.48 ng/dl, and the analytic sensitivity is less than 0.4 ng/dl.

Thyroid-stimulating hormone assay

Architect TSH assay is a CIMA for the quantitative determination of TSH in human serum and plasma. The reagent kit used is 7K62. The default result is expressed in $\mu\text{IU/ml}$ ($\times 1 = \text{conc. in mIU/l}$). The normal range is 0.35–4.94 $\mu\text{IU/l}$, and the analytical sensitivity is less than 0.01 $\mu\text{IU/l}$. The total T3 and T4 were not included in the study.

Postoperative variables

The level of inotropic support, durations of operation, ICU stay, and total hospital stay, postoperative arrhythmia mainly AF, and renal impairment were documented. Clinical follow-up of neurological status was carried out.

Statistical analysis

All data were analyzed using the SPSS software for analyzing and extracting the *P*-value for the collected data. The data were expressed as numbers, percentages, and mean \pm SD. A probability value (*P*-value) less than 0.05 was considered statistically significant. Comparison of mean \pm SD in two groups was carried out using the Student *t*-test, whereas within-group comparison during the study period was carried out using Friedman's analysis of variance test.

Results

The demographic data showed no significant differences between both groups with respect to the age or other clinically associated states. There was a high lipid profile than normal in both groups (Table 1).

Changes in the cardiac function and hemodynamics

There was no significant difference in the preoperative EF% in both groups ($P < 0.71$). The intraoperative EF% measured using TEE showed significant myocardial depression in group B when compared with preoperative EF ($P < 0.003$), whereas there was very minimal changes in group A. There was a statistical significance intraoperatively in group B compared with group A ($P < 0.001$). In intragroup comparison in both groups, the 12 h postoperative EF% measured using TTE showed almost the same changes as that of intraoperative EF until 24 h, but there was a statistical significance between both groups ($P < 0.001$). After 24 h of operation, the effect of thyroxine started to appear in both groups with a marked improvement in the cardiac functions, with weaning of inotropes, and obvious increase in the mean arterial blood pressure (MAP). In group B, the EF% after giving the Eltroxine improved from $37.51 \pm 3.07\%$ at 12 h after operation to $45.64 \pm 2.0\%$ at 24 h after operation and then to $53.76 \pm 7.7\%$ just before hospital discharge (Table 2).

The intraoperative MAP was markedly decreased in group B to 57 ± 8 and was still low after 12 h of operation, despite the maximum inotropic support or even the use of intra-aortic balloon counterpulsation (IABP). There was a statistical significance between both groups ($P < 0.004$). MAP was markedly improved 24 h postoperatively and just before hospital discharge (103 ± 23 and 107 ± 24 , respectively) after Eltroxine supplementation (Table 2).

The inotropic support was mainly adrenaline, and it showed a significant increase in group B compared with group A ($P < 0.007$). In group A none had IABP inserted, whereas in group B IABP was inserted in three patients who had severe hemodynamic instability, despite the high adrenaline dose (Table 3).

The level of thyroid hormones

The preoperative thyroid profile in all patients in both groups showed insignificant difference between both groups, with normal free T3 and T4 and high TSH, which showed a range of 7–11 $\mu\text{IU/l}$.

The intraoperative values (measured at the end of the procedure) showed little changes in the level of T4 in

Table 1 Demographic data

	Group A (<i>n</i> = 47) [<i>N</i> (%)]	Group B (<i>n</i> = 40) [<i>N</i> (%)]	Intergroup <i>P</i> -value	SS (<i>P</i> < 0.05)
Age	53.60 \pm 9.3	53.37 \pm 8.88	0.49	SI
Sex (male)	39 (83)	35 (85)	0.48	SI
Diabetes	20 (42)	17 (42.5)	0.35	SI
Hypertension	21 (45)	17 (42.5)	0.42	SI
Dyslipidemia	36 (77)	31 (77.5)	0.96	SI
Smoking	26 (55)	21 (52.5)	0.61	SI

Values are presented as mean \pm SD for age and ratio and as number of patients for sex and risk factors. SS, statistically significant.

Table 2 Changes in the cardiac function and hemodynamics

	Group A (n = 47)	Group B (n = 40)	Intergroup <i>P</i> -value	SS (<i>P</i> < 0.05)
EF%				
Preoperative	51.7 ± 7.03	51.4 ± 9.6	0.71	SI
Intraoperative	49.08 ± 4.17	36.9 ± 3.1	0.001	SS
12-h postoperative	50.8 ± 6.8	37.5 ± 3.07	0.001	SS
24-h postoperative	52.3 ± 7.8	45.6 ± 2	0.09	SI
At discharge	53.9 ± 8.13	53.7 ± 7.7	0.8	SI
MAP				
Preoperative	95 ± 19	98 ± 23	0.25	SI
Intraoperative	97 ± 18	57 ± 8	0.004	SS
12-h postoperative	101 ± 20	66 ± 11	0.004	SS
24-h postoperative	105 ± 21	103 ± 2	0.085	SI
At discharge	108 ± 23	107 ± 2	0.099	SI

Values are presented as mean ± SD. EF, ejection fraction; MAP, mean arterial blood pressure; SS, statistically significant.

Table 3 Postoperative data

	Group A (n = 47) [N (%)]	Group B (n = 40) [N (%)]	SS (<i>P</i> < 0.05)
IABP	0	3 (7.5)	SS
Inotropes (mean)	0.018 µg/kg/min	0.16 µg/kg/min	SS
AF postoperative	4 (8.5)	8 (20)	SS
AF at discharge	0	0	–
Chest infection	0	4 (10)	SS
Renal impairment	0	2 (5)	SS
Perioperative MI	0	1 (2.5)	SS

AF, atrial fibrillation; IABP, intra-aortic balloon counterpulsation; MI, myocardial infarction; SS, statistically significant.

both groups. The level of T3 remained almost within normal range in group A (2.44 ± 0.9 pg/ml), but a marked decrease was recorded (0.9 ± 0.3 pg/ml) in group B ($P = 0.002$). The level was corrected 24 h postoperatively, after the intake of Eltroxine, to 2.3 ± 0.8 pg/ml and then to 2.5 ± 1.1 pg/ml before hospital discharge. The level of TSH was markedly increased in group B intraoperatively (14.3 ± 4.7 µIU/l), and it was near normal in group A (6.6 ± 1.4 µIU/l) ($P = 0.0073$ between both groups). The predischarge values of the thyroid profile were almost equal in both groups, with no significant statistical differences, and they were normal. The TSH started to decrease in both groups after intake of Eltroxine in hospital ($P = 0.97$) (Table 4).

Postoperative data

The total time of operation showed no significant difference in both groups, whereas the ventilation time was longer in group B because of delayed recovery (group A: 3.7 ± 0.5 h; group B: 19.1 ± 1.4 h; $P < 0.006$). The ICU stay was longer in group B because of the delayed recovery and the high inotropic supports (group A: 1.3 ± 0.5 days; group B: 3.9 ± 1.3 days; $P < 0.006$). The total hospital stay in group B was longer than in group A (group A: 4.9 ± 0.5 days; group B: 9.1 ± 0.6 days; $P < 0.001$).

Of the four patients in group B, one patient had chest infection in the form of bronchopneumonia and

three patients had bronchopneumonia; all recovered well without any squeal. In group A, none had chest infections. Two patients in group B had renal impairment with high creatinine level (>3 mg/dl), but none had dialysis and all recovered. None of the patients in group A had renal problems. Four cases in group A and eight cases in group B had postoperative AF; all recovered from AF and discharged sinus rhythm. None of the patients in group A had perioperative MI, whereas one patient in group B had inferior MI, but he recovered well. None of the patients in both groups had cerebrovascular strokes. We did not have intraoperative or in-hospital mortality in both groups. No conversion to CPB was required in both groups.

Discussion

The cardiovascular system is an important target for the thyroid hormones. Hypothyroidism decreases the oxygen and substrate utilization by all major organs; the most important effect of the thyroid hormones on the cardiovascular system is the increased peripheral vascular resistance and myocardial depression, together with accelerated atherosclerosis [12].

There is a definite relationship between clinical hypothyroidism and increased mortality and morbidity after cardiac surgery, especially on-pump surgeries, and it is more prevalent in the female sex groups at old ages [13]. Despite the increased incidence of mortality and morbidity with clinical hypothyroidism, little is clear about the subclinical states (SCHT). The most known is its relationship with high AF incidence. However, until now there are no clear recommendations to give preoperative thyroxine to those patients for decreasing the incidence of postoperative AF [14].

In our cardiac center, in 2006, we had problems in CABG in three patients. When we operated those patients who had fair EF%, one patient developed rapid AF at the end

Table 4 The level of thyroid hormones

	Group A (n = 47)	Group B (n = 40)	Intergroup P-value	SS (P < 0.05)
T3 (pg/ml)				
Preoperative	2.53 ± 1.1	2.49 ± 1.0	0.5	SI
Intraoperative	2.44 ± 0.9	0.9 ± 0.3	0.002	SS
24-h postoperative	2.6 ± 1.2	2.3 ± 0.8	0.4	SI
At discharge	2.7 ± 1.2	2.5 ± 1.1	0.5	SI
T4 (ng/dl)				
Preoperative	1.3 ± 0.2	1.2 ± 0.19	0.1	SI
Intraoperative	1.2 ± 0.18	1.1 ± 0.15	0.1	SI
24-h postoperative	1.29 ± 0.2	1.25 ± 0.2	0.13	SI
At discharge	1.1 ± 0.4	1.2 ± 0.5	0.1	SI
TSH (μIU/l)				
Preoperative	10.8 ± 3.3	9.0 ± 3.2	0.1	SI
Intraoperative	6.7 ± 1.7	14.3 ± 4.7	0.007	SS
24-h postoperative	6.8 ± 1.4	8.2 ± 2.2	0.9	SI
At discharge	7.3 ± 1.4	7.7 ± 0.5	0.97	SI

Values are presented as mean ± SD. SS, statistically significant; TSH, thyroid-stimulating hormone.

of the surgery, and unexplained tachycardia was observed in other two patients. The three patients had significant hypotension, and the myocardium appeared significantly depressed. The flow in the grafts was measured using a flow meter, and it was good in all grafts in the three patients. We supported them with IABP and the maximum inotropic supports. The first patient died 17 h postoperatively due to persistent hypotension and uncontrollable arrhythmias; the only positive thing in his investigations was the disturbed thyroid profile. The other two were investigated using electroencephalography, brain computed tomography scan, and thyroid profile for the hemodynamic instability and delayed recovery. We discovered low T3 and T4 with high TSH; hence, we gave them thyroxine early after 6 h of surgery and they improved and survived. Preoperatively, the thyroid profile was not performed as a routine test, and those patients were apparently euthyroid. After analysis of those cases in depth, we discovered a high rate of SCHT, and we decided to perform routine thyroid profile in all patients admitted for cardiac surgery. In addition, we decided to conduct our study to explore this issue.

SCHT is a debatable clinical state, in which patients have no specific symptoms and most of them do not receive treatment. Furthermore, most of them do not know about this illness. It easily progresses to clinical hypothyroidism; even if not occurred, many complications may occur with SCHT. Hence, McDermott and Ridgway [15] in their study recommended to treat SCHT to decrease the complications and to avoid frank clinical state.

Those patients with SCHT when subjected to stress, major surgeries, or emergency surgeries without being known to have SCHT might have more disturbed TSH, T3, and T4 or even clinical hypothyroid state, which will be difficult to diagnose during or just after the surgery. A delayed recovery has been reported in a case of Chilaiditi's

syndrome by Sharma [16]. Chilaiditi's syndrome is internal herniation of the intestine into the subdiaphragmatic space. Patients subjected to cardiac surgery, not necessarily open heart, may show this disturbance [16].

In our study, we operated using off-pump to avoid the significant effects of CPB on the thyroid profile and the postoperative complications related to hypothyroidism. Some authors had stated these effects of CPB on the thyroid function and the hazards leading to myxedema after the surgery; yet, there were known history of hypothyroidism [17]. This proved the effects of CPB on the thyroid profile, but we had a group of patients with SCHT, which should be investigated even without the use CPB.

The effect of CPB on patients with frank hypothyroidism receiving thyroxine preoperatively was investigated and proved equal outcomes with a control group of normal patients. [18] It is known that CPB induces 50% decrease in free T3 and 75% decrease in total, whereas TSH remains normal for 24 h and then it is normalized as long as the hypothalamic — thyroid axis is normal (euthyroid sick syndrome). This phenomenon also occurs with the off-pump procedures [19,20].

Although some authors showed that there is no significant effect of preoperative control on SCHT and others found a high rate of postoperative morbidity related to this, namely AF and renal impairment, they did not declare the operative course after giving thyroxine to those patients; this was carried out in our cases discovering its value.

As our study on hypothyroidism was conducted in the endemic areas, there were many cases of SCHT. We had an early problem in such patients of SCHT, who were not receiving thyroxine; they had stormy operative and postoperative courses. We found that performing routine thyroid profile preoperatively is a must, as many

patients of SCHT may be missed or undiagnosed. It is not a real problem in clinical hypothyroidism, which is easily suspected, but it is a problem in patients with SCHT, who are apparently normal. Hence, screening of these hormones preoperatively is vital.

The preoperative intake of thyroxine even in asymptomatic patients had a great effect on the operative course, as we had stable patients with low heart rate and fair MAP and still maintained good EF. However, patients who did not receive thyroxine had high heart rate, AF, and low MAP, necessitating IABP and high inotropic support.

There was no doubt about the effect of SCHT on the recovery from anesthesia, which was significantly delayed with high inotropic support postoperatively because of the suppressed myocardium leading to low MAP and low EF% when exposed to the surgery. The intake of thyroxine in group B had markedly improved the recovery of the cardiac efficiency with a marked improvement in the MAP, EF%, and a decrease in the heart rate. Those patients who received thyroxine preoperatively showed an eventless smooth operative and postoperative course, whereas the operative and postoperative course was stormy in other patients and they recovered only after giving thyroxine.

The total ventilation time, the ICU stay, and the total hospital stay were higher in the second group, which increased the hospital and the patient's costs and exposed the patients to mortality and morbidity unnecessarily. The incidence of AF was higher in the patients who did not receive preoperative Eltroxine, with an increased rate of other postoperative complications (renal impairment, chest infection, and perioperative MI).

Conclusion

Routine preoperative thyroid profile in patients admitted for cardiac surgery is a must, and despite the debate about the value of thyroxine in patients with SCHT, at least those patients admitted for cardiac surgery having SCHT should receive thyroxine supplementation 48 h preoperatively.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

References

- 1 Topliss DJ, Eastman CJ Diagnosis and management of hyperthyroidism and hypothyroidism. *Med J Aust* 2004; 180:186-193.
- 2 Khandelwal D, Tandon N Overt and subclinical hypothyroidism: who to treat. *Drugs* 2012; 72:17-33.
- 3 Pluta RM, Burke AE, Glass MA Subclinical hypothyroidism. *JAMA* 2010; 304:1402.
- 4 Gillet M Subclinical hypothyroidism: subclinical thyroid disease: scientific review and guidelines for diagnosis and management. *JAMA* 2004; 291:228-238.
- 5 Cooper DS Subclinical hypothyroidism. *N Engl J Med* 2001; 345:260-265.
- 6 Biondi B, Palmieri EA, Lombardi G, Fazio S Effects of subclinical thyroid dysfunction on the heart. *Ann Intern Med* 2002; 137:904-914.
- 7 Vanderpump MP, Tunbridge WM, French JM, *et al.* The incidence of thyroid disorders in the community: a twenty year follow-up of the Wickham survey. *Clin Endocrinol (Oxf)* 1995; 43:55-68.
- 8 Marqusee E, Haden ST, Utiger RD Subclinical thyrotoxicosis. *Endocrin Metab Clin North Am* 1998; 27:37-49.
- 9 Paschen U, Muller MJ, Darup J, Kalmar P, Seitz HJ Alteration in thyroid hormone concentration during and after coronary bypass operation. *Ann Endocrinol (Paris)* 1983; 44:239-242.
- 10 Aslan A, Osmanagaoglu S, Cavolli R, Emiroglu O, Kahraman D, Uymaz OK, *et al.* Sodium nitroprusside infusion prevents hypothyroidism in patients undergoing coronary artery bypass grafting: a prospective randomized clinical trial. *J Cardiovasc Med (Hagerstown)* 2010; 11:575-582.
- 11 Jyrala A, Gatto NA, Kay GL Incidence of subclinical hypothyroidism in cardiac surgery patients. Comparison of presentation characteristics, hospital and medium-term outcomes with euthyroid patients. *World J Cardiovasc Surg* 2012; 2 3:55-59.
- 12 Klein I, Danzi S Thyroid disease and the heart. *Circulation* 2007; 116:1725.
- 13 Zindrou D, Taylor KM, Bagger JP Excess coronary arteries bypass graft mortality among women with hypothyroidism. *Ann Thorac Surg* 2002; 74:2121-2125.
- 14 Park YJ, Yoon JW, Kim KL, Lee YJ, Kim KW, *et al.* Subclinical hypothyroidism might increase the risk of transient atrial fibrillation after coronary artery bypass grafting. *Ann Thorac Surg* 2009; 87:1846-1852.
- 15 McDermott MT, Ridgway EC Subclinical hypothyroidism is a mild thyroid failure and should be treated. *J Clin Endocrinol Metab* 2001; 86:4585-4590.
- 16 Sharma SM Case report: undiagnosed subclinical hypothyroidism associated with Chilaiddit's syndrome affecting anesthetic management. *Anesth Pain Intensive Care* 2012.
- 17 O Connor CJ, March R, Tuman KJ Severe myxedema after cardiopulmonary bypass. *Anesth Analg* 2003; 96:62-64.
- 18 Syed AU, El Watidy A, Bhat AN, Wahba A, El Okley R, Kiyani A Coronary bypass in patients with thyroxin replacement therapy. *Asian Cardiovasc Thorac Surg* 2002; 10:107-110.
- 19 Clarke RE Cardiopulmonary bypass and thyroid hormone. *Ann Thorac Surg* 1993; 56Suppl:S35-S41; discussion S41-S42
- 20 Velissaris T, Tang AT, Wood PJ, Hett DA, Ohri SK Thyroid function during coronary surgery with and without cardiopulmonary bypass. *Eur J Cardiothorac Surg* 2009; 36:148-154.