Therapy with L-thyroxine and Omnadren after Cardiac Surgery. A Case Report.

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Abstract

Background: Cardiopulmonary bypass in cardiac surgery produces systemic inflammatory response and catabolic state. Severe stress frequently causes abnormalities in thyroid hormones in the absence of primary thyroid disease, defined as sick euthyroid syndrome (SES).

Materials and methods: Supplementation therapy with thyroid and anabolic hormones in combination with an adequate nutritional support has been used to improve outcome in critically ill patient after cardiac surgery.

Results: Administration of thyroid and anabolic hormones significantly improved patient’s condition.

Conclusions: Supplementation therapy with thyroid and anabolic hormones in combination with an adequate nutritional support could be used to improve hemodynamics, achieve transition to anabolic metabolism and enhance recovery, which could eventually help for a reduction in post-operative morbidity and mortality.

Keywords
anabolic metabolism, cardiac surgery, L-thyroxine, nutrition, testosterone

INTRODUCTION

After cardiac surgery using cardiopulmonary bypass, abnormalities in the circulating thyroid hormone levels could be found in the absence of a primary thyroid disease: so called sick euthyroid syndrome (SES). It is still unclear whether SES should be interpreted as an adaptive mechanism or a marker of the illness severity and whether treatment should be initiated in these patients. On the other hand, thyroid hormones have effects on the cardiovascular system that make them an attractive option for some patients after cardiac surgery.1

Low circulating testosterone levels (<12 nmol/L) could contribute to an increase in the incidence of cardiovascular risk factors and deterioration of glucose metabolism.2 Rodent studies demonstrate that after ischemic reperfusion injury, testosterone may exhibit both protective and negative cardiac effects. Its rapid substitution has a depressive effect on myocardial function3, whereas its chronic administration in physiological doses reduces the size of the infarct zone, improves contractility, reduces arrhythmias, improves myocyte viability and autonomic regulation after myocardial damage4.
CASE REPORT

A 71-year-old woman with suspicion of ascending aorta dissection is admitted to the Cardiosurgery Clinic with the following comorbidities: anemia and hyperuricemia; recurrent atrial fibrillation; arterial hypertension grade II; heart failure NYHA classes III; duodenal ulcer; type 2 diabetes mellitus (non-insulin dependent); polyneuropathy and hepatosteatosis. Previously the patient had an uneventful aortic valve replacement (AVR) in 2010.

The patient was regularly taking the following medications: acenocumarol 3 mg, bisoprolol 2x5 mg, rosvastatin 10 mg, valsartan 2x160 mg, metformin 3x426 mg (blood sugar levels kept between 8 and 12 mmol/L). Preoperative results: TSH 0.45 (0.4 - 4.65 mcIU/ml), fT4 0.98 (0.89-1.76 ng/dl), testosterone level 10.0 (9.90 - 27.80 nmol/L).

The diagnosis of ascending aortic aneurism with dissection was confirmed by the preoperative echocardiography (Fig. 1) and computed tomography (CT).

After an informed consent, the patient was considered for an emergency surgery of the ascending aorta. The operation went uneventfully under extracorporeal circulation with flow rate of 3.80 - 4.56 L/min, ECC 105 min, aortic cross-clamping time (ACT) 33 min, reperfusion time of 49 min. A cold antegrade cardioplegia (Kirklin) 2000 ml was delivered under pressure to the heart. Selective antegrade cerebral perfusion was not necessary in this patient. After debridement of pericardial adhesions the aortic aneurysm was visualized - starting from the aortotomy and reaching the root. The size of the ascending aorta was 45 mm. A longitudinal aortotomy was performed. On inspection the aortic valve prosthesis was functional and intact. There was a false lumen starting from the old aortotomy. The entry was closed with a 4/0 suture and the false lumen obliterated. The aortotomy was closed with 3/0 prolene.

After the end of operation, the patient was transferred to ICU on high doses of catechol amines (dopamine 14 mcg/kg/min, adrenaline 10 mcg/kg/min). Six hours after the operation a furosemide infusion 80 mg/hr was initiated (creatinine 158 mcmol/l, urea 11.54 mmol/l, oliguria, CVP +13 mmHg). 24 hours later was started CVVHDF and dobutamine infusion 5 mcg/kg/min.

On day 3 postoperatively the patient was started on enteral feeding with Nutricomb Energy HP 500 (B. Braun, Melsungen, Germany) which was gradually increased to 2000 ml/day. The patient was extubated on day 8 after operation and transferred to a cardio-surgery HDU bed.

Sixteen days postoperatively due to deteriorated respiratory function the patient was reintubated and readmitted to the ICU. Chest X-ray didn’t show signs for an infection. On day 18 postoperatively a therapy with levothyroxine 100 mcg/day was administered, TSH 2.45 (0.4 - 4.65 mcIU/ml), fT4 0.78 (0.89-1.76 ng/dl).

On day 26, a tracheostomy was performed and testosterone level was checked – 6.80 (9.90-27.80 nmol/L). On day 27 postoperatively testosterone (Omnadren) 250 mg was given (SHBG 48 nmol/L and testosterone 0.93 nmol/), and a second and third application of the same dose of the hormone was administered one and two weeks later, respectively.

Thirty-three days after operation the echocardiography (Fig. 2) showed improvement with atrial flutter 130/min, CVP +5 mmHg and dopamine infusion 3 mcg/kg/min.

The patient was discharged from ICU fifty-five days after operation with improved general condition. He was discharged from the hospital 70 days postoperatively, gaining weight and well mobilized. On a one month follow-up, she resumed her usual daily physical activity.
DISCUSSION

Thyroid hormones affect oxygen consumption and calcium, phosphorus, carbohydrate, protein and lipid metabolism. There are significant changes in cardiovascular function when there is shift in their blood levels. It is well known that several severe diseases can cause abnormalities in the circulating thyroid hormone levels in the absence of primary thyroid disease - sick euthyroid syndrome (SES).  

Most commonly, there is a decrease in total and unbound tri-iodothyronin (T3) with normal levels of thyroid stimulating hormone (TSH) and thyroxin (T4). This is classified as SES type 1 (SES-1) or low-T3 syndrome. The de-iodination from T4 to T3 in the liver is impaired, leading to a decrease of biologically active T3. Inflammatory cytokines have been linked to the development of SES and the levels of cytokines seem to influence the severity of the condition. Additionally, tissue-specific thyroid hormone bioactivity is reduced during cellular hypoxia which contributes to the low T3 syndrome in severely ill patients. In general, the severity of illness correlates to the severity of SES.  

In some severely-ill patients there might be a dramatic fall in total T3 and T4 levels, this state is called the low-T4 syndrome or SES type 2 (SES-2) and has a poor prognosis. T4 metabolism may be further influenced by a decrease in thyroid binding globulin levels.  

In both SES-1 and SES-2, serum levels of TSH are impaired and do not increase in response to low T3 or T4 levels. In some patients TSH level could even decrease which is associated with increased morbidity and mortality. Additionally, the response of TSH to thyroid releasing hormone (TRH) is impaired in SES.  

SES has a significant impact on outcome and survival. In their cohort of 573 patients, Iervasi and colleagues found that low levels of free T3 were the highest independent predictor of death, especially in cardiac patients.  

T3 administration is associated with improved hemodynamics, reduced peripheral vascular resistance and increased cardiac output, suggesting the potential benefit of thyroid hormone replacement.

Androgen replacement therapy

Essentially, any significant injury or illness will activate a catabolic stress response and its outcome is strongly influenced by the ratio of the catabolic to the anabolic processes, the duration of the catabolic state and the therapeutic measures aimed at correcting the condition.  

The stress response is characterized by increased levels of the hormones epinephrine and cortisol, which increase energy demands beyond needs and cause increased protein breakdown, primarily for the production of excess glucose used as an energy source. Moreover, levels of endogenous anabolic hormones like human growth hormone (HGH) and testosterone are decreased. The abnormal hormonal environment leads to a net increase in degradation of muscle and visceral protein. Breaking down protein over the long-term is known to be maladaptive and autodestructive.  

Testosterone is the natural endogenous androgen. The importance of testosterone is evidenced by the complications seen with low testosterone levels, and these are sarcopenia or loss of lean mass, increased rate of development of osteoporosis, anemia, skin thinning, impaired wound healing, and general weakness.  

Testosterone levels decrease with any severe stress. Testosterone replacement is essential in hypogonadal states and is typically done by depot injection. However, beyond replacement therapy, testosterone is not used as an anabolic agent as it has relatively weak anabolic activity compared to its analogs and its androgenic side effects can become problematic. Testosterone has no effect on the inflammatory process or on glucose metabolism. The major complications with its use are a decrease in high-density lipoproteins, some fluid retention, and endrogenic effects.

Anabolic steroids like omnadren refer to the class of drugs produced by modification of testosterone. The intention in this case was to take clinical advantage of the anabolic effects of testosterone while decreasing the androgenic side effect of the naturally occurring molecule thus enhancing the patient’s recovery. On the other hand, it has to be highlighted that hormone replacement therapy is still a controversial issue in cardiac surgery and the modern treatment of patients undergoing cardiac operations provides an excellent postoperative care with short ventilation times, short length of stay and low morbidity and mortality in the majority of clinical cases. Nevertheless, clinically significant SES can be detected, especially with long bypass times. T3 supplementation in these patients could prove beneficial. To demonstrate a significant clinical effect of T3 administration, large numbers of patients specifically at risk for SES and low cardiac output syndrome are needed and the study must include patients at specifically at risk for SES and low cardiac output syndrome. Treatment protocols in these patients, however, often include routine inotropic support and afterload reduction as well as open chest strategies, thus, common outcome parameters such as hours of ventilation, use of catecholamines, blood pressure, urine output, and so on may prove difficult to assess.

There is a complex relationship between hormones, nutrition and protein synthesis, anabolism and protein degradation, which is often destabilized under stress. There is an increase in catabolic (cortisol and epinephrine) levels and decrease in the levels of anabolic hormones (HGH and testosterone), resulting in increased protein degradation and decreased protein synthesis. As a result there is a self-destructive response, which in some cases could be fatal. It has been found that use of certain anabolic agents could help neutralize catabolism and restore hormonal balance.
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CONCLUSION

Supplementation therapy with thyroid and anabolic hormones in combination with an adequate nutritional support could be used to improve hemodynamics, achieve transition to anabolic metabolism and enhance recovery, which could eventually help for a reduction in post-operative morbidity and mortality.

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Материалы и методы: Заместительная терапия тиреоидными и анаболическими гормонами в сочетании с адекватным питанием использовалась для улучшения исхода у критически больного пациента после операции на сердце.

Результаты: Введение тиреоидных и анаболических гормонов значительно улучшило состояние пациента.

Выводы: Заместительная терапия тиреоидными и анаболическими гормонами в сочетании с адекватным питанием может использоваться для улучшения гемодинамики, достижения перехода к анаболическому метаболизму и улучшения выздоровления, что, в свою очередь, может помочь снизить послеоперационную заболеваемость и смертный исход.

Ключевые слова
L-тироксин, тестостерон, кардиохирургия, питание, анаболический метаболизм