Effects of Intravenous Triiodothyronine During Coronary Artery Bypass Surgery

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ABSTRACT

A prospective randomized and double-blind study was performed to evaluate whether perioperative triiodothyronine administration has any effect on cardiovascular performance after coronary artery bypass surgery. Sixty patients were assigned to 2 groups of 30 each. When crossclamping ended, group A received an intravenous bolus of triiodothyronine, followed by infusion for 6 hours. Group B received a placebo. Serum triiodothyronine levels and hemodynamic parameters were serially measured. Mean postoperative cardiac index was slightly, but not significantly, higher in group A, whereas systemic vascular resistance was significantly lower in group A. Compared with preoperative values, serum triiodothyronine levels dropped significantly in group B at the end of cardiopulmonary bypass and remained low 12 hours postoperatively, while levels rose significantly in group A. No significant differences were detected between the groups in the incidence of arrhythmia, the need for inotropic support, intensive care unit stay, mortality, and morbidity. Perioperative administration of triiodothyronine increased cardiac output slightly and decreased systemic vascular resistance, but it had no effect on operative outcome. Routine use after coronary surgery is thus not recommended.

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INTRODUCTION

Thyroid hormone metabolism has been shown to be altered during cardiopulmonary bypass (CPB), resulting in the reduction of serum concentration of the hormone. This reduction may contribute to hemodynamic instability during the early postoperative period.[1,2] It is unknown if reduced serum triiodothyronine (T_3) levels contribute to ventricular dysfunction after open heart surgery or if intravenous T_3 has acute inotropic effects in this setting. In a number of clinical studies, cardiac output increased in patients undergoing coronary artery bypass grafting (CABG) who received intravenous T_3, but no significant improvement in operative outcome was observed.[1,3] Despite this, its use has been advocated in certain situations, such as prophylaxis of atrial fibrillation (AF) or to improve cardiac output in patients who are difficult to wean off CPB.[4–6] The aim of this study was to determine whether intravenous T_3 administration improves hemodynamics, the incidence of arrhythmia, and the outcome after CABG.

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PATIENTS AND METHODS

Between January 1998 and June 2001, 60 patients undergoing CABG were recruited for a prospective double-blind study, of which 30 received intravenous T_3 (Thyrotardin-inject; N Hennig, Berlin, Germany) (group A) and the other 30 a placebo (group B). There were no differences between the groups in age, left ventricular function, and the number of bypasses made. Patients over 75 years of age, under thyroid hormone therapy, or undergoing reoperation, concomitant procedures, or emergency surgery were excluded. Informed consent was obtained from each patient. Demographic data are shown in Table 1.

All patients were operated by the same surgeon. Anesthesia was induced with 5 mg midazolam, 10 $\mu g \cdot kg^{-1}$ fentanyl citrate, and 0.1 $mg \cdot kg^{-1}$ vecuronium bromide and maintained with a combination of fentanyl citrate and vecuronium bromide. Diltiazem infusion was started with the induction of anesthesia and continued in the intensive care unit. Hemodynamic monitoring was conducted via a Swan-Ganz catheter. Myocardial protection was achieved by tepid antegrade and retrograde cardioplegia and the single-clamp technique. T_3 levels were measured before and immediately after CPB was established.

Table 1. **Demographic and Operative Data**

Variable	Group A (n = 30)	Group B (n = 30)
Age (years)	64 ± 5	66 ± 10
Gender (males/females)	19/11	18/12
LVEF (%)	33 ± 7	35 ± 8
Left main CAD	5	4
Preoperative T_3 ($ng \cdot dL^{-1}$)	80 ± 20	81 ± 23
No. of distal anastomoses	2.9 ± 0.9	2.8 ± 0.7
CPB time (min)	78 ± 11	81 ± 9
ACC time (min)	51 ± 8	50 ± 9

ACC = aortic crossclamp, CAD = coronary artery disease, CPB = cardiopulmonary bypass, LVEF = left ventricular ejection fraction.

After the crossclamp was removed, group A patients received an intravenous bolus of T_3 of 0.8 $\mu g \cdot kg^{-1}$, followed by infusion of 0.113 $\mu g \cdot kg^{-1} \cdot h^{-1}$ for 6 hours postoperatively, while group B patients received a placebo. Hemodynamic and serum T_3 measurements were made at the end of CPB and 6 and 12 hours postoperatively. Postoperative T_3 measurements were made in 10 patients in each group because of cost. During weaning, when necessary, patients received a standard dose of epinephrine–norepinephrine infusion (0.01 to 0.05 $\mu g \cdot kg^{-1} \cdot min^{-1}$) for inotropic support. Operative data are shown in Table 1.

Two-sample t test was used to evaluate demographic, baseline, and time variables. Intergroup comparative variables were analyzed with chi-squared test or Fisher's exact test. Two-tailed analysis of variance was used to compare continuous variables at multiple time points. A p value < 0.05 is considered as significant. Mean values are expressed as mean ± standard deviation.

RESULTS

Serum T_3 concentrations were normal in both groups before surgery (Table 1). However, they decreased significantly during surgery and remained low 12 hours postoperatively in group B. In group A, serum T_3 rose beyond normal levels throughout T_3 infusion and returned towards normal values 12 hours postoperatively (Table 2).

Although group A had a slightly higher mean postoperative cardiac index than group B at the end of CPB, the difference was not statistically significant. Systemic vascular resistance (SVR) in group A was significantly lower than in group B at the end of CPB. There were no significant differences between the groups in the heart rate, mean arterial pressure, central venous pressure, and pulmonary capillary wedge pressure (Table 2). Minimal inotropic support (0.01 to 0.03 $\mu g \cdot kg^{-1} \cdot min^{-1}$) was required by 75% of group A patients and 78% of group B patients during weaning off CPB, with no significant difference

Table 2. **Hemodynamic Data and Serum T_3 Levels**

	Post-CPB		6 Hours Later		12 Hours Later	
Variable	Group A (n = 30)	Group B (n = 30)	Group A (n = 30)	Group B (n = 30)	Group A (n = 30)	Group B (n = 30)
HR ($beats \cdot min^{-1}$)	95 ± 2	93 ± 5	98 ± 3	100 ± 4	101 ± 12	98 ± 14
MAP (mm Hg)	80 ± 10	82 ± 8	79 ± 6	80 ± 8	80 ± 7	82 ± 6
CVP (mm Hg)	7 ± 2	7 ± 3	8 ± 2	9 ± 2	7 ± 3	8 ± 3
PCWP (mm Hg)	10 ± 4	8 ± 3	9 ± 2	10 ± 1	8 ± 3	7 ± 2
CI ($L \cdot m^{-2} \cdot min^{-1}$)	2.75 ± 0.52	2.63 ± 0.6	2.7 ± 0.2	2.6 ± 0.1	2.7 ± 0.1	2.7 ± 0.2
SVR ($dyne \cdot s \cdot cm^{-5}$)	1,040 ± 220†	1,350 ± 420†	1,100 ± 100	1,280 ± 190	1,190 ± 100	1,200 ± 90
T_3 ($ng \cdot dL^{-1}$)*	122 ± 14	41 ± 11	134 ± 12	34 ± 16	97 ± 8	58 ± 11

*Serum T_3 concentration was measured in 10 patients in each group. †p < 0.001 (Fisher's exact test). All other comparisons not significant. CI = cardiac index, CPB = cardiopulmonary bypass, CVP = central venous pressure, HR = heart rate, MAP = mean arterial pressure, PCWP = pulmonary capillary wedge pressure, SVR = systemic vascular resistance, T_3 = triiodothyronine.

between the groups. Six hours later in the intensive care unit, 42% of group A patients and 46% of group B patients continued to receive inotropes. There was no significant difference in the incidence of arrhythmia between the groups: 3 patients in group A and 4 in group B had AF. The surgical course and clinical outcome did not differ between the groups. Postoperative outcome is summarized in Table 3.

DISCUSSION

Poor cardiac performance is a major cause of morbidity and death in patients who undergo open heart surgery, especially older patients and those with extensive disease and poor ventricular function.[7,8] Improving perioperative management is thus vital. Because of recent evidence that CPB results in altered thyroid hormone metabolism, interest is focused on the relationship between decreased serum T_3 levels and hemodynamics after CPB.[9] The mechanism by which serum T_3 concentrations decrease during CPB is not certain, but it is probably due to hypothermia, hemodilution, and the activation of inflammatory-response mediators.[10,11]

Similarities exist between hypothyroid patients and those undergoing cardiac surgery in that serum T_3 levels and cardiac contractility decrease while peripheral vascular resistance increases. Although studies have shown that perioperative T_3 treatment may improve outcome in patients with postoperative cardiac dysfunction, this is not a widely accepted therapy.[3,6,12] Several largely uncontrolled studies found that T_3 administration reduced perioperative mortality and the need for inotropic agents after CABG.[2,12] The results of our trial, however, do not support these conclusions.

Our results, like many others, suggest that T_3 may act acutely as a cardiotonic agent. It raises cardiac output and lowers SVR.[13] However, whether this is related to its direct positive inotropic effect or to peripheral vasodilation is unknown.[14] In our series, the fall in SVR was evident, but a significant increase in cardiac output was not observed. T_3 treatment did not lower the incidence of AF in our study, in contrast to the results of other series.[6]

Routine assessment of thyroid function before CPB has been proposed, but it has not gained wide acceptance. Nevertheless, some still support routine assessment in elderly female patients.[15] As thyroid hormone affects the adrenergic system and since most CABG patients are treated with exogenous catecholamines, clinicians must be aware of patients with hyperthyroidism or thyroid storm.[5]

Despite promising experimental evidence, clinical trials have so far not demonstrated conclusively the benefits of T_3 repletion in CABG patients. However, anecdotal evidence supports its use as a rescue agent in weaning off CPB or as a prophylactic for AF.[5,13,16]

In this study, the administration of T_3 during cardiac surgery led to only negligible enhancement of cardiovascular performance and no reduction in inotropic requirement or the incidence of arrhythmias. Neither was there any improvement in terms of intensive care unit stay, the duration of mechanical ventilation, hospital stay, mortality, and other major complications. Therefore, although T_3 did not cause any adverse effects, our findings do not support the routine use of T_3 during cardiac surgery.

Table 3. **Postoperative Outcome and Complications**

Variable	Group A (n = 30)	Group B (n = 30)
Intensive care unit stay (days)	1.7 ± 0.5	1.9 ± 0.3*
Mechanical ventilation (hours)	11 ± 7	12 ± 6*
Hospital stay (days)	8.1 ± 1.2	8.2 ± 1.5*
Mortality	0	0
Complications		
Pulmonary	1	2
Neurologic	0	0
Renal	0	0
Infection	1	1
Atrial fibrillation	3	4
Bleeding	2	3

*Not significant between groups (chi-squared, Fisher's, and t tests).

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