Section: Cardiothoracic and Vascular Surgery

Original Research Article

EFFECT OF CARDIOPULMONARY BYPASS ON THYROID HORMONE LEVELS IN PATIENTS UNDERGOING ON-PUMP VERSUS OFF-PUMP CARDIAC SURGERY

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Abstract

Background: The use of (CPB) cardiopulmonary bypass during cardiac surgery is associated with changes in thyroid hormone levels. Using Off-pump coronary artery bypass grafting (OPCAB) for coronary revascularisation in patients with coronary artery disease appears more physiological than on-pump coronary artery bypass grafting (ONCAB). Whether these modalities of treatment have a significant effect on thyroid hormone levels needs to be investigated further. **Aim**: To evaluate the effect of cardiopulmonary bypass on thyroid hormone levels in patients undergoing on-pump versus off-pump cardiac surgery. **Material and Methods:** fT3, fT4 and TSH were measured sequentially pre-operative, immediate post-operative, and then at 1/6/24 hours duration in 2 groups of patients. The first group (52) underwent on-pump versus the second group (52) off-pump coronary artery bypass grafting after applying inclusion and exclusion criteria. **Results:** In both groups, fT4 and TSH were within normal limits. There was a sequential non-significant decline in fT4 levels during 24 hrs postoperatively. Mean fT3 levels were below the normal range. **Conclusion:** There was no significant difference in thyroid hormone levels between the off-pump and on-pump coronary artery bypass surgery.

INTRODUCTION

The use of CPB during cardiac surgery is associated with changes in thyroid hormone levels. This phenomenon can be ascribed as a euthyroid sick syndrome. [1-3] In Euthyroid sick syndrome there are normal TSH, total T4 (TT4), and free T4 (fT4) levels while total T3 (TT3) and free T3 (fT3) levels are decreased. De-iodination of T4 to its active compound T3 decreases while levels of the inactive reverse rT3 increase. [4] Controversy in the literature exists about whether this denotes true hypothyroidism. The alternative theory suggests that thyroid hormone fluctuations may be an adaptation to traumatic stress. During the stress of surgery due to increased oxygen expenditure body merely decreases catabolic expenditure as a self-defense mechanism. [5] The effect of T3 administration during or after CPB in animal and clinical studies has met with debatable results. [6-10] Euthyroid sick syndrome is associated with other general surgery procedure. [11-12] Serum thyroid hormone fluctuations are seen in both ONCAB and OPCAB patients akin to the euthyroid sick syndrome. [13-16]

Aim

The primary aim was to study the association of thyroid hormone levels in patients undergoing coronary artery bypass surgery on or off a cardiopulmonary bypass machine pump.

MATERIALS AND METHODS

Sample size of 104 primary elective CABG patients were included, who offered informed consent and met the study criteria. [Table 1]

The research was approved by the IMS, BHU INSTITUTIONAL ethics committee. All operations were performed by the same set of surgeons and

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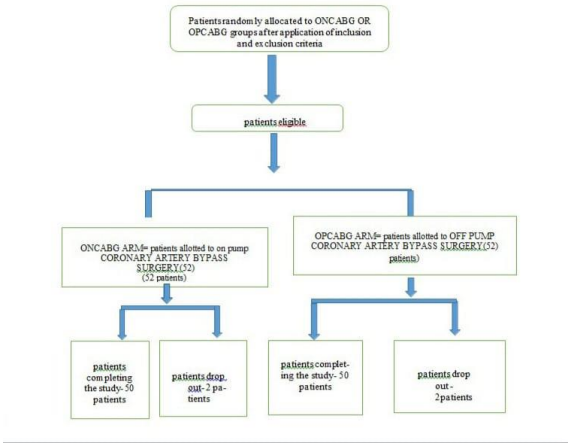
there were no medical reasons to impede OPCAB. The individuals were allocated into TWO groups randomly with a computer-generated algorithm: ONCABG(n=52) or OPCABG(n=52). (Figure1) Sample size computation was based on data from an earlier survey that explored thyroid hormone changes undergoing CABG on pump versus off-pump.[14] To observe a 25 pg/dL variance in fT3 between both cohorts using a t-test at 24h post-operatively with p=0.05 and beta=0.9, the sample size required was 104 patients. 24-hour time-frame was preferred as it is when fT3 attains its lowest postoperative level. [2, 3, 14]



Aspirin was taken until the day and clopidogrel or ticagrel was discontinued 5days before the surgery. All patients were prescribed with low molecular weight heparin (0.4/0.6ml based on body-weight), twice a day from admission to the pre-operative day, and discontinued 12 hours before the procedure. An anesthetic protocol used in all cases consisted of fentanyl, benzodiazepine, and vecuronium as a muscle relaxant. The goal was to maintain mean arterial pressure of above 60mmHg and cardiac index (CI) exceeding 2.2L/min m^2. As required, dopamine was used as an inotropic agent, while phenylephrine or norepinephrine injections and NTG continuous infusion served as vasoconstrictors and coronary vasodilators respectively.

In the ONCAB patients group, CPB was set up by a single two-stage venous cannula inserted into via the right atrium into the inferior vena cava. An arterial cannula was placed in the ascending aorta. The circuit was primed with 1000 mL of sterofundin solution, 500 mL of gelofusine, and 4500 IU of sodium heparin. Additional heparin, as required to maintain the activated clotting time (ACT) above 480sec. CPB with the pulsatile flow during aortic cross-clamping was conducted under mild core hypothermia (35.8C), using a hollow-fiber membrane oxygenator (541BMedtronic Affinity NT, parkway, Minneapolis, USA) and arterial line filtration (D734 Micro 40, Sorin Biomedica, Gloucester, UK). Intermittent antegrade cold blood cardioplegia (4 degree C) delivered through a 12G aortic root cannula was used for myocardial protection. The cardioplegic solution consisted of 20% StThomas'Hospital No.2 solution (Martindale Pharmaceuticals, Essex, UK). A dose of 12ml/kg was delivered to induced diastolic cardiac arrest and a maintenance dose of 2-3 ml/kg was administered after the completion of each distal anastomosis. Flow was maintained at 2.5 L/min m^2 to maintain the mean perfusion pressure between 60 and 80mmHg.

All cases were accessed for surgery by a median sternotomy, before harvesting suitable conduits. Systemic heparinisation was implemented to reach a target ACT of 400 seconds. To keep the operative area still during coronary anastomosis, a mechanical tissue stabilizer (Octopus; MedtronicLtd, Watford, UK) based on suctioning was employed. Blower mister was used sparingly to assist during distal anastomosis primarily at the area of the arteriotomy. Intracoronary shunt (Flo-Thru; Biovascular Inc., Minnesota, USA) was introduced inside the arteriotomy to maintain myocardial perfusion.

Blood samples were collected from the radial artery shortly after induction and later at the conclusion of the operation, as well as 1, 6, and 24 hours postoperatively. These samples were centrifuged, then frozen for further examination. Thyroid hormones fT3, fT4, and TSH were measured using a chemiluminescence system.

The results are computed as the mean standard deviation. Patient data in the two groups were compared using Student's t-test. Categorical variables were compared using Fisher's exact test. A paired t-test was used for intra-group comparison. Because the data contained subgroups (ONCAB vs OPCAB), The Statistical Package for Social Sciences (SPSS) version 15 software was used for the analysis. A p-value of less than 0.05 was considered statistically significant.

Table 1: Exclusion criteria

Number of exclusion criteria	Exclusion criteria
1.	Age ≥ 75 years
2.	Liver failure/ (hepatic enzymes or bilirubin above normal range)

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3.	Left ventricular ejection fraction < 50%
4.	Previous Cerebro vascular accident.
5.	Renal failure (eGFR <90 ml/min)

RESULTS

The demographic variables between the two groups are shown in. [Table 2]

Table 3 shows the intra-operative data along with the outcome. No significant differences were encountered in outcomes between the two groups. No MACE (major adverse cardiovascular events) such as MI, cerebrovascular accidents, end-organ damage, or death were observed. [Table 3]

TSH (Thyroid-stimulating hormone) levels were within the normal range in all subjects. No significant baseline differences were noted between the groups (p = 0.97). There was a decline in TSH levels during early postoperative hours, with nadir reaching 6 hours post-op. At 24 hours, the levels partially normalized to preoperative levels.

There was no difference in baseline levels of free thyroxine between the groups (p=0.89) and remained normal.

No baseline significant difference was observed in free tri-iodothyronine (fT3) levels between the groups (p=0.17). FT3 levels declined in all subjects with the lowest value found at 24hours. FT3 levels at 24h were below the normal range with significant difference noted among the groups (p<0.01) for both groups. [Table 4]

Table 2: Patient characteristics

Variable	ONCAB(n=52)	OPCAB(n=52)	P VALUE
AGE	78.4±12.8	75±15.7	0.34
GENDER			0.86
MALE	45	48	
FEMALE	6	4	
CCS ANGINA CLASS			0.67
I	15	11	0.45
II	28	32	
III	2	4	
IV	7	5	
PREVIOUS MI	23	27	0.49
HYPERTENSION	29	35	0.88
MORBID OBESITY	6	9	0.97
EUROSCORE	2.9±1.3	3.2±0.7	0.78

Table 3: Intraoperative data and clinical outcome

VARIABLE	ONCAB(n=52)	OPCAB(n=52)	P VALUE
DISTAL ANASTOMOSIS	2.7±0.6	2.2±0.7	0.11
CPB TIME(MIN)	90 ± 14.8		
AOCLX TIME(MIN)	59± 11.7		
TIME TO EXTUBATION (MIN)	7.7± 2.5	6.8±1.9	0.17
ICU LENGTH OF STAY(DAYS)	4.2±3.2	3.5±2.5	0.25
PERIOPERATIVE LOW C.I.	2	2	1.2
SUPRAVENTRICULAR ARRHYTHMIA	21	17	0.35
WOUND INFECTION	8	10	0.87
PNEUMONIA	11	8	1.34

Table 4: Perioperative thyroid hormone levels in the two groups

Variable	Pre op	At end of procedure	Postophour1	Postophour6	Post op hour 24
TSH(mU/L)					
ONCAB	2.41±2.34	2.35±2.12	1.40±1.20	1.18±0.88	1.72±1.56
OPCAB	2.62±1.41	1.99±1.12	1.57±0.88	1.10±0.49	2.17±1.50
fT4(pmol/L)					
ONCAB	15.40±2.30	15.9±1.58	15.67±2.40	13.22±1.65	14.21±2.15
OPCAB	15.55±2.15	17.99±4.10	15.98±2.34	11.98±2.98	13.67±1.91
fT3(pmol/L)					
ONCAB	5.14±0.53	4.65±0.56	4.54±0.48	3.67±0.23	3.31±0.34
OPCAB	5.09±0.67	4.67±0.67	3.98±0.78	3.12±0.78	3.34±0.78

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DISCUSSION

Significant thyroid hormone changes after CPB was found in the present study similar to reports in the literature.[1-3,15] The post-surgical euthyroid sick syndrome appears during the postoperative period when the patient is catabolic,[17-18] which suggest that euthyroid sick syndrome works as an adaptive device to lessen catabolism,[2,4] not being a real hypothyroid state.

Thrush et al, [14] compared thyroid function in low-risk patients under normothermic (35.1 degree C) and hypothermic (26.5-degree celsius) nonpulsatile CPB, yet no significant differences were found between the groups. This is concurrent with Lehot et al, [17-19] who also found no variation in thyroid hormone levels among those using such CPB technique in 20 individuals. It is considered unlikely that haemodilution due to priming volume was a major factor influencing postoperative alterations of thyroid hormones, as albumin levels return to their initial state after 2hr, but thyroid levels fluctuated for a few days. [1, 2, 14]

Despite consideration for haemodilution, Bremner et al. still reported an euthyroid sick response in their findings.[15] Indications suggest that haemodilution does not play a main role in altering thyroid hormone concentration,[2] but absence of pulsatile flow does play a role. Buket et al compared pulsatile versus non- pulsatile flow. [3, 16, 17, 20]

Careful examination of the evidence suggests that haemodynamic factors and the stress of surgery are likely to be the main determining elements of thyroid axis response, rather than hypothermia and haemodilution in CPB. It is notable that pulsatile flow during CPB is an important factor.[3,15,21] Hence OPCAB produced a thyroid response similar to that found with CPB; transient declines in cardiac output and pressure experienced during distal anastomoses have been well documented,[22-24] with instances of right ventricular dysfunction due to cardiac manipulation.

This study design ensured homogeneity of the groups, which is sinequanon of randomized controlled trials with limited sample size. The behaviour of patients with poor left ventricular function, pre-existent thyroid disease, uncontrolled diabetes mellitus, or extracardiac arteriopathy may differ, and it should form basis of further studies in this domain.

CONCLUSION

This study highlights thyroid hormone level changes during OPCAB and ONCAB. This finding is consistent with the post-surgical euthyroid sick syndrome. Use of mildly hypothermic pulsatile CPB for short periods of time is not responsible for the development of euthyroid sick response.

Additional Information

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. Institute of medical sciences, BHU-Institutional ethical committee issued approval ECR/526/INST/UP/2014/RR-20. The study title" Cardiopulmonary bypass induced electrolyte imbalance, correction and implications inoperative and intensive care unit management in patients undergoing on pump cardiac surgery." submitted by Dr. Ratnesh Kumar has been approved by institutional ethical committee.

Animal subjects: All authors have confirmed that this study did not involve animal subjects or tissue.

Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following:

Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work.

Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work.

Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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