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Sick Euthyroid Syndrome a Prognostic Indicator in Acute Myocardial Infarction

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Abstract

Introduction: Sick Euthyroid syndrome is linked with alteration in thyroid function. It is seen in many non-thyroidal illnesses. But its major implications are seen in Acute Myocardial Infarction. Abnormalities of thyroid function tests are seen in this condition. These abnormalities include a decrease in free T3 or both a decrease in FT3 and a decrease in free T4. This has shown to be as a marked prognostic indicator in this Acute Myocardial Infarction. Sick Euthyroid syndrome is contemplated to be 'benign'. It has been shown for increased morbidity and mortality. This is the reason why this is considered as prognostic marker. Hence the study was conducted to assess the thyroid function in Acute Myocardial Infarction and its further link with immediate out come of patients with Acute Myocardial Infarction.

Methods: 50 Consecutive patients of Acute Myocardial Infarction admitted in our institute was our study group. A thorough history, complete clinical work-up, detailed systemic work-up was done. Further investigations such as 2 D Echo to assess left ventricular function, multiple electrocardiograms and Creatinine phosphokinase-MB levels were done. In addition to this from total T3, T4 and TSH were done. These were taken 24-36 hours after onset of chest pain on day. Reports were taken again on day 7.

Results: The mean age for males was 58±12 years and 61±9 years in females. The male: female ratio was 2.1:1. There was no significant difference in the mean values of T3, T4 and TSH on days 1 and 7. Statistically significant association which is $p<0.05$ was observed between the day 1 serum T3 and CK-MB, cardiogenic shock, acute complications and decreased Left ventricular ejection fraction.

Conclusion: Abnormal thyroid function in Acute Myocardial Infarction is a poor prognostic indicator. It indicates poorer cardiac function in form of decreased left ventricular ejection fraction. Thus this leads to increased mortality. The sick-euthyroid syndrome is characterized as a decreased free T3 levels that occur in a setting of non-thyroidal illness without any thyroid or hypothalamic-pituitary dysfunction. It most frequently is seen in patients with MI, and is associated with a higher mortality.

Keywords: Sick Euthyroid Syndrome; Myocardial Infarction.

Introduction

Thyroid hormone plays a crucial part in the cardiovascular system function. It also helps to maintain the cardiovascular homeostatic mechanism. Alteration in the thyroid function actually affects mortality in patients with Acute Myocardial infarction.

The thyroid hormones play a vital role in the normal functioning and homeostasis of all the systems in the body. But the most immensely affected system is the cardiovascular system. It has

to bear maximum impact of thyroid dysfunction. The biologically active form of thyroid hormone is Tri-iodothyronine (T3). It is T3 which plays an important role in modifying the rate of heart and the ability of heart to contract. It also affects the peripheral arterial resistance [1,2]. A slight alteration in thyroid function affects the function of ventricles, serum cholesterol levels, and heart rate and rhythm is linked with greater cardiovascular mortality. The biologically active form of thyroid hormone T3 acts by binding with specific nuclear receptors. This further leads to stimulation of responsive genesencrypting for structural and functional cardiac proteins. In addition to this direct, extranuclear as well as non-transcriptional effects have also been described [3-5]. Thus any alteration in thyroid function may in any way affect the cardiovascular system.

Cardiovascular diseases such as acute myocardial infarction, heart failure, CABG, stress cardiomyopathy cause alteration in thyroid function. Certain non-thyroidal diseases like starvation, sepsis, surgery and bone marrow transplantation cause thyroid dysfunction [6-10]. Such as tate of thyroid dysfuction due to non thyroid illness is often characterized as "sickeuthyroid syndrome" (SES). It is usually associated with decreased total T3 and/ or free T3. It also shows increased reverse T3, and normal TSH, T4 and free T4 level.

This syndrome causes significant morbidity as well as mortality specially in patients with acute myocardial infarction.

Material and Methods

Cross sectional observational study conducted at out institute. With 18.8% expected reduction in serum T3, precision of 10%, desired C.I. of 95%, the minimum sample size calculated was 50. were included in the study.

Exclusion Criteria-

Drug history of amiodarone, corticosteroids, thyroid disease drugs.

Receiver of iodinated contrast agents in last 2 weeks.

Pre-existing thyroid diseases, cancer chronic lung disease, chronic liver failure and chronic renal failure, systemic sepsis and uncontrolled diabetes mellitus (DM).

People not giving consent.

Inclusion Criteria

Consecutive patients suffering from acute myocardial infarction.

Acute myocardial infarction was diagnosed with help of detailed history taking, Cardiovascular system examination and acute biomarkers which rise in Acute myocardial infarction. The record of patients was noted till the time of discharge/ death. Complications like arrhythmias, heart failure, cardiogenic shock, ventricular aneurysm werenoted. Following investigations were done in patients –

- Consecutive ECGs,
- CPK - MB taken at admission,
- Lipid profile (fasting) and
- 2D - echocardiography

The left ventricular ejection fraction (LVEF) was evaluated on basis of 2D-ECHO findings. Thyroid profile (total T3, T4, TSH) was done on Day 1 of chest pain and again on Day 7 from 1st day. The first sample collected 24-36 hrs. Thyroid hormone values (total T3, T4 and TSH) were calculated by using chemilluminescent immunoassay 10 MAX 410 monobind IMNA.

With above methodology results were formulated.

Results

52 consecutive patients of acute myocardial infarction were studied. However 2 patients needed to be excluded as their day 7 thyroid profile could not bedone as they suffered from pneumonia during their hospital stay. Thus the final study group included 50 patients.

Table 1: Age & gender distribution of patients

Age (years)	Male (n=38)	Female (n=12)	Total (n=50)
20-30	1 (2.1%)	0 (0%)	1 (1.3%)
31-40	3 (6.9%)	1 (4.3%)	4 (8.3%)
41-50	9 (15.2%)	2 (8.6%)	11 (18.1%)
51-60	12 (20.8%)	4 (47.8%)	16 (36.2%)
61-70	10 (16.6%)	3 (21.8%)	13 (23.7%)
>71	2 (6.9%)	1 (17.3%)	5(12.5%)
Total	37 (100%)	11 (100%)	50 (100%)
Mean Age	55.51±12.32 (30-85)	60.13±9.80 (40-80)	57.98±11.71 (30-85)

The mean age was 55.51±5.87 years in males and 60.13±9.80 years in females. The male : female ratio was 2.1 (Table 1).

Table 2: Consecutive T3, T4 and TSH levels measured on day 1 and day 7

Mean Thyroid Hormone level	Day 1 Mean±S.D.	Day 7 Mean±S.D.
Serum T3 (ng /ml)	0.86±0.34	0.92±0.31
Serum T4 level (mcg/dl)	7.01±2.07	6.96±2.05
Serum TSH level (mcIU/ml)	2.12±1.55	2.08±1.46

The mean T3, T4 and TSH levels measured on days 1 and 7 were within normal limits (Table 2).

Table 3: Distribution of study subjects according to various parameters and Day 1 Serum T3 levels

Parameters		Day 1 Serum T3 (ng/ml)		
		<0.52	0.52-1.9	>1.9
CPK-MB (IU/L)	< 150 (n=39)	6 (9.9%)	32 (88.5%)	1 (1.6%)
	>150 (n=11)	6(54.5%)	5(45.5%)	0(0%)
Cardiogenic shock	Present (n=5)	5(100%)	0(0%)	0(0%)
	Absent (n=45)	8(11.7%)	36(86.8%)	1(1.5%)
LVEF	=40 (n=10)	2(40%)	8(60%)	0(0%)
	>40 (n=40)	2(4.2%)	37(93.7%)	1(2.1%)
Complications	Present(n=21)	12(60%)	9(40%)	0(0%)
	Absent (n=29)	0(0%)	28(98.1%)	1(1.9%)
Mortality	Non- survivors (n=4)	4(100%)	0(0%)	0(0%)
	Survivors (n=56)	8(11.7%)	47(86.8%)	1(1.5%)

For further examination, a random cut-off of 150 IU/L was considered for CPK-MB and 40% was taken for LVEF, as it indicates poor systolic LV function. Statistically significant association was observed for CK-MB levels (p=0.001), LVEF < 40% (p=0.000), cardiogenic shock (p=0.000), complications (p=0.000) and mortality (p=0.000) (Table 3).

Discussion

The following study was conducted to evaluate the role of thyroidin Acute Myocardial Infarction. The mean T3, T4 and TSH levels on day 1 were normal. The results showed no significant difference on consecutive estimation.

CPK-MB, indicates the scope of cardiac injury. It was inter related with T3 (day 1) in this study. A cut-off value of 150 IU/L was taken. This indicator had positive association with the T3 level which was significant. Similar findings were made by Rajappa et al[11] and Friberg et al. [12-13]. The pathogenesis of SES includes production of inflammatory cytokines. There are various Inflammatory cytokines such as Interleukin-6 (IL-6). These are produced by the cardiac myocytes in the border zone of re-perfused viable myocardium, monocytes and macrophages. Now these inflammatory cytokines appear to constrain the hepatic mono - iodinase activity. This hepatic mono-iodinase activity is responsible for peripheral translation of T4-T3. Now this rise in cytokines levels is directly proportional to the amount up to which the myocardium has been damaged and has been necrosed. This in turn is also revealed by the measured CK-MBlevels from the patients.

Thyroid dysfunction is seen in subjects suffering with AMI. It presents as fall in the levels of T3 / free T3 and normal values of T4 and TSH.

There is a positive linkage of LVEF with day 1 serum T3 in the present study which was significant. A comman adverse prognostic factor is that of low LVEF in AMI. Similar observations have been noted by Rajappa et al. [11] Lymvaios et al. [12], Friberg et al. [13]. The reason for this is that the thyroid hormones control the amount of calcium in the sarcoplasmic reticulum necessary for systolic contraction. Thus any reduction in thyroid hormones in turn affects the systolic function. In addition to this high peripheral vascular resistance may further lead to the increased LV work load. This will result in LV dysfunction.

In the present study, low day 1 serum T3 correlated positively with the morbidity (acute complications) as well as mortality in AMI. Friberg et al. [13], Pimentel et al. [16] have similarly noted higher short term as well as long term major adverse cardiac events (MACE) and mortality in AMI patients with SES.

Definition of "Euthyroid sick syndrome" or "low T3 syndrome" consists of decreased levels of FT4, FT3, and TSH. This may underestimate euthyroid sick syndrome and the mortality associated with thyroid abnormality in CCU patients.

Thus SES in AMI may not be a 'benign' response as it is associated with pooreroutcome.

Conclusion

This study was done to evaluate the relation between thyroid function and Acute Myocardial Infarction. Significant association was observed between day1 serum T3 and LV systolic function. Patients of AMI with life threatening complications had comparatively lower levels of. Thus patients with AMI with sick euthyroid syndrome are at a higher risk of death and deranged thyroid function acts as a marker for poor prognosis.

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