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Original Research Article

Evaluation of Cold Pressor Response in Patients with Hypothyroidism

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ABSTRACT

Introduction: Numerous studies have shown that the hypofunctional abnormalities of the cardiovascular system are due to the influence of deficient autonomic outflow associated with thyroid hormone deficiency. So an attempt has been made to study the sympathetic activity in hypothyroid patients when exposed to cold stress.
Material and Methods; Systolic Blood pressure (BP) and diastolic blood pressure before and during cold pressor test performance were evaluated and recorded in 30 hypothyroid patients (age group 20-50 years) and the results were compared with age and sex matched controls (Euthyroids) group. Hypothyroidism was confirmed by biochemical findings. Data analysis was done using student's 't' test using SPSS software.
Results: During cold stress, Systolic blood pressure and Diastolic blood pressure values were significantly less (P = 0.000) in hypothyroid patients when compared to the control group.
Conclusion: The results suggested that autonomic function changes do occur when exposed to cold stress in hypothyroid patients. Precautions have to be taken to prevent the development of autonomic failure in hypothyroid patients.

***Key words*:** Hypothyroidism, Autonomic dysfunction, Sympathetic nervous system, Cold pressor test, Coronary endothelial cell.

INTRODUCTION

Human being can perceive different degrees of thermal sensation. For distinguished cold sensation, Cold receptors are located under the skin at discrete separated spots. The Extreme degree of cold may provoke a stimulation of pain receptors and fibers. [1] Thus a painful cold sensation can develop a psychological state that triggers the response in the sympathetic nervous system and release norepinephrine. Extensive sympathetic discharge excites the cardiovascular systems that produce pressor response, i.e, arteriolar constriction, increase heart rate, increase stroke volume, and increase cardiac output and blood pressure. [2] Hence, to assess the sympathetic activity in a subject, simple vasomotor test called the cold pressor test was done. This test was developed by Hines EA in 1936. [3] Recent studies have found that in response to the cold stress, there is increased sympathetic discharge throughout the body. [4] The Sympathetic and parasympathetic division of autonomic nervous system have individual and antagonistic actions, which can regulate and modulate the involuntary functions of the body. Changes in cardiovascular variables such as heart rate and blood pressure are regulated by changes in the activity of sympathetic and parasympathetic nervous system. The thyroid hormones also play a major role in the regulation of ionotropic; rhythmic

properties of the cardiac muscle and peripheral vascular resistance. [5] They mediate their actions on myocardium in both extracellular and intracellular level. Extracellularly they change the function of plasma membrane and may also activate the extra nuclear sites on the myocardium. At the intracellular level they stimulate specific nuclear receptors on the myocardium, to alter actions in the production of specific mRNAs.

On the other side, they may also modulate the β -adrenergic receptor function by increasing their number, so that there is a change in responsiveness of myocardium to sympathetic stimulation. [6,7] Recently, the incidence of thyroid dysfunctions has increased and become a common health problem. [8] The prevalence of hypothyroidism is 1:100 but if the patients with sub clinical hypothyroidism are included it becomes 5:100. 4.6% of world population are affected by hypothyroidism. Thyroid disorders in India affect 42 million people. In hypothyroidism the male: female ratio is 1:6 to 8. [9] Some recent studies have been reported that 95% hypothyroidism cases are related to primary hypothyroidism. Women with small body size at birth and low BMI during childhood are most commonly suffering from hypothyroidism. In India 6% of the adult population are suffering from hypothyroidism. The prevalence of congenital hypothyroidism in India has been reported to be 1 in 2640. [10] Lekakis et al, [11] Dagre A et al [12] in their study reported that in thyroid hormone deficiency, the endothelium is damaged at peripheral vasculature levels which may impair vascular function. Endothelial dysfunction of peripheral vasculature is an important feature of atherogenesis. [13] Egashira K et al [14] concluded that the rise in heart rate and systolic blood pressure in cold stress is due to sympathetic stimulation. Moreover, serum thyroid stimulating hormone (TSH) levels have been found to be inversely correlated with endothelium-dependent dilatation. [12] Taddei S, et al [15] assessed that in subclinical hypothyroid patients the endothelial dysfunction is caused by reducing nitric oxide (NO) availability. Nitric oxide is a signaling molecule that raising cGMP levels to relaxes vascular smooth muscle. [16]

Cold stress stimulates the coronary endothelial cell to release NO. Recent study done by Hiroi Y et al [17] suggested that thyroid hormones i.e. mainly T_3 stimulates the enzymes responsible for the synthesis of nitric oxide in endothelial cells. So thyroid dysfunction is attributed to changes in capacities for the formation and response to NO. [18] When exposed to extremely cold conditions a physiological stress response is activated to maintain body homeostasis. Cold pressor test induces stress so that there was a change in cardiovascular activity in order to maintain body homeostasis. [19] During stress condition a surge of catecholamine hormones like epinephrine, norepinephrine and the main stress hormone of the body cortisol is released. These hormones binding with the adrenergic receptors, thus they support the sympathetic response system to increase heart rate and vasoconstriction to increase blood pressure. [20]

In a cold stress test for maintaining constant body temperature the blood flow to the hand is decreased to reduce heat loss to the cold. Sympathetic nervous activity during cold stress increases cardiac output to increase capillary filtration rate in muscle tissue to the supplying the nutrients and oxygen to the muscular tissue and also allow for increase muscle to contract. Heart rate and blood pressure will be measured in the cold pressor test is to determine the level of stress response in the body. It is based on the reflex pathway where the afferent limb is somatic fibers where as the efferent limb is sympathetic fibers. The cold pressor test is an ethical and efficient way to affect the sympathetic response. [21]

MATERIALS AND METHODS

The study was carried out in the departments of Physiology, Narayana

Medical College and Superspeciality Hospital, Nellore in the year 2009 - 2010. After obtaining institutional ethical committee clearance relevant clinical history was obtained from the patients. A Cold pressor test was conducted on 30 hypothyroid patients (age group 20-50 years). The patients were selected on the basis of laboratory findings of a normal free T_3 and T_4 levels and TSH more than 5 mI U/L, the results were compared with age and sex matched controls (Euthyroids) who were non teaching staff of Narayana Medical College Nellore. Written consent was obtained from all the subjects.

Materials

The requirements for this study are -

1. A container filled with ice water with a temperature of 2-4°C.
2. A mercury-in-glass thermometer to measure the temperature of water.
3. Sphygmomanometer.

Method

1. Proper instructions should be given to the subject and explain them this test would not cause any harm.
2. Ask the subject to sit comfortably on a stool and the examiner should record the resting blood pressure.
3. Ask the subject to immersion hand in cold water, record the BP from the other hand, at 30 second intervals for a period of 2 minutes after that the subject is allowed to remove the hand. Tell them to withdraw the hand at any time if the cold is too painful.
4. Measure the maximum increase in systolic and diastolic blood pressure.
5. The data recorded from the hypothyroid patients should be compared with the normal group.

Statistical analysis

Data was analyzed using SPSS version 20, Chicago, USA. Categorical data were expressed as actual numbers. Continuous data were expressed as Mean and Standard Deviation. Categorical data were analyzed using the Chi - square test. Continuous Parametric data (age) were analyzed using unpaired 't' test. Non-Parametric data (total score) was analyzed using Mann - Whitney 'u' test. A two tailed probability of < 0.05 was considered as statistically significant.

RESULTS

In our study, the comparison of mean values of standard autonomic function test i.e., cold pressor test in control and patients (Table 1) shows that highly significant (P = 0.0000) changes in autonomic nervous system activity seen in Hypothyroid patients (Table-1).

T here was a highly significant (P = 0.0000) difference between the SBP, DBP values in response to cold stress in both hypothyroid and control group (Table-2 & 3).

Table: 1 showing SBP and DBP values in test and control groups

S.No	Parameters	Controls Mean ±SD	Test group Mean ±SD	P - Value
1.	CPT (SBP beforehand immersion)	121.0±4.51	109.9 ±5.59	0.000
2.	CPT (SBP during hand immersion)	133.9 ±4.02	116.9 ±5.69	0.000
3.	CPT (DBP beforehand immersion)	75.4 ±5.73	71.5 ±7.46	0.000
4.	CPT (DBP after hand immersion)	88.07 ±7.25	73.97 ±9.70	0.000

CPT = Cold Pressor Test, SBP = Systolic Blood Pressure, DBP = Diastolic Blood Pressure

Table2: Difference in SBP before and after cold press or test

S.No	Status	Mean	Standard Deviation	P Value
1.	Hypothyroid group	-6.933	7.2916	0.000
2.	Control group	11.9	5.7316	

Table3: Difference in DBP before and after cold press or test

S.No	Status	Mean	Standard Deviation	P Value
1.	Hypothyroid group	-2.433	2.7753	0.000
2.	Control group	12.666	4.028	

Table 2 showing SBP difference values in hypothyroid and control group

Table 3 showing DBP difference values in hypothyroid and control group

DISCUSSION

Various effects on the heart and peripheral vascular system like heart rate, blood pressure, ventricular systolic and diastolic functions of heart etc, are

maintained by thyroid hormones. [5] During the performance of the cold pressor test (CPT) a vascular sympathetic response, increased peripheral resistance and a sustain increased BP is observed in normal subjects. [22] A change in the blood pressure is due to sympathetic activity than vagal. So we chose to do this study to observe the cold stress on the autonomic activity in hypothyroid patients. The results of our study highlight the effect of thyroid deficiency on sympathetic activity.

In our study we observe that in the control group, the mean systolic blood pressure was significantly increased from 121.0 mm of Hg (Resting SBP) to 133.9 mm of Hg (during immersion of hand).similarly the diastolic blood pressure 75.4 mm of hg (resting) and 88.07 mm of hg (during immersion of hand). And in the hypothyroid patients the mean systolic blood pressure of was slightly increased from 109.9 mm of Hg (Resting SBP) to 116.9 mm of Hg (during immersion of hand). There is a mild increased Diastolic blood pressure from 71.5 mm of Hg (during resting) from 73.97 mm of Hg (during immersion of hand) in hypothyroids. This is due to sympathetic insufficiency of myocardium and peripheral resistance and is statistically significant.

Like other systems in the body the functions of autonomic nervous system are impaired in the absence of thyroid hormones. Thyroid hormone directly affected the vascular smooth muscle to reduce resistance in peripheral arterioles to decreased mean arterial pressure. Indirectly they activate the renin-angiotensin-aldosterone system to increase renal sodium absorption, erythropoietin synthesis from kidney to increase blood volume and preload. [23]

In Hypothyroidism condition the cardiac contractility, cardiac output, blood pressure and systemic vascular resistance (SVR) are changed. [24]

The change in SVR is due to endothelial dysfunction and impaired VSM relaxation. [25] The measurement of blood pressures during stress shows that there is a decrease in sympathetic tone in hypothyroid group. So this may be taken as comprehensive evidence that there is a high possibility of autonomic dysfunction in thyroid hormone deficiency. Several pathophysiological mechanisms have been proposed for this. When exposed to cold stress, there is a sympathetic reflex response act as a protective phenomenon to reduce heat loss from the body. It also increases the secretion of stress hormone and catecholamine's from adrenal gland, thereby body homeostasis are maintained. Increase in blood pressure during cold stress is due to increased cardiac output with increased muscle sympathetic nerve activity. [26] This leads to increase peripheral resistance [27] Studies done by Seals [28] indicating that there is an increased sympathetic discharge to skeletal muscle than blood pressure. Difference in SBP and DBP values before and after cold pressor test (table no. 2& table no. 3) were significantly less in hypothyroid patients when compared to control group.

Our results are also correlate with the study done by Sushil et al [29] they concluded that in hypothyroids the sympathetic reflex is unaffected but that values are slightly decreased. However, deficient thyroid hormones are associated with increased hypercholesterolemia [30] and changes in cardiac gene expression [23] all this may lead to change in cardiac contractility, cardiac output and blood pressure in these patients.

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