Original Article:

Assessment of Autonomic Functions in Hypothyroidism

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Abstract: Disturbances in autonomic functions have been observed in many diseases including hormonal disorder (Banisters 1983). Present study was undertaken to study the autonomic functions in thyroid hormones on in 60 untreated hypothyroid patients, using Valsalva and deep breath test, cold pressor test, hand grip test and orthostatic test to assess the sympathetic and parasympathetic reflexes. The results obtained in this study were compared with the age sex matched controls. It is concluded that the sympathetic response is not altered in the hypothyroid cases while reflex vagal activity is significantly reduced.

Key Words: Autonomic Function, Hypothyroidism, Hormone

INTRODUCTION: Thyroid hormones produce various effects on heart and peripheral vascular system causing changes in heart rate and blood pressure, ventricular systolic and diastolic function of the heart[2]. Several studies have been carried out to understand the mechanism of altered cardiovascular functions due to increased thyroid secretion in animals and humans[2,3,4,5] but no studies have been conducted on hypothyroid patients till date.

Levey et al[3] in 1990 have reported that excess thyroid hormones causes hyper adrenergic state without changing the serum catecholamine level suggesting that increased heart rate in hyper thyroid is attributed to the hyperactive sympathetic system due to sensitization of cardiac catecholamine receptors. Earlier reports by Howitt[6] in 1968, Vander Schoot[7] in 1965 and Grossman[8] in 1971 indicated that sensitivity of cardiac catecholamine receptors remains unchanged in spite of excess thyroid hormones in both experimental animal and human.

The site of action for thyroid hormones is also likely to be in the central nervous system for reducing the vagal tone in hyper thyroid states because iodothyronine compounds have been isolated from various parts of nervous system including hypothalamus and medulla. In studies[5] to elicit baroreflex in hypothyroid patient, it was found that the cardiac vagal motor neurons were at a low excitability state and baroreflex sensitivity was considerably low. This fact indicated that thyroid hormone might have action on CNS structure which integrates autonomic function and behavior. It is surprising that although there are extensive studies in hyperthyroid states to understand the activity of thyroid hormone on autonomic function but studies in hypothyroid states are still lacking.

MATERIAL AND METHODS: The subjects of the present study were selected from the patients attending the O.P.D. of Endocrinology division of Medicine department in Sir Sunder Lal Hospital, BHU. Fresh untreated, clinically diagnosed or suspected patients from either sex, without any complications or associated diseases, were material for the present study. The patients were carefully examined and history of the illness was taken before bringing them to physiology department, Institute of Medical Sciences (BHU) for further evalution of autonomic functions.

A total of 106 patients were screened for the present study; of which only 30 subjects having specific clinical signs & symptoms suggestive of depressed thyroid activity were included in the present study. The subjects presenting with any other complication apart from thyroid

disorder were not included in the study. Subjects who had received any treatment with respect of thyroid or any other relevant organic diseases were also discarded. A group of 30 age and sex matched controls were also subjected to the same tests to compare the autonomic response of the study group.

METHODOLOGY:
All subjects from the control as well as study group selected for the present study were asked to perform following procedures to assess their autonomic response.

Valsalva maneuver (Valsalva 1704) to record the Valsalva ratio as per the protocol described by Levin9 in 1966 for assessment of parasympathetic functions.

Deep breath test for assessment of vagal efferent pathway, Orthostatic test using the method as described by Roser Bannister1 in 1988 to evaluate the activity of both sympathetic and parasympathetic systems.Handgrip test to assess the efferent sympathetic pathway

Cold pressure test was also performed in the subject to observe any change in the heart rate and blood pressure before and after the maneuver (sympathetic response).

Serum T3, T4 and TSH levels were also estimated using standard radioimmunoassay kits in all the 60 subjects to assess the thyroid function quantitatively.

All the data obtained from controls as well as hypothyroid patients during the study was tabulated and analyzed statistically using t test and chi square test.

RESULTS: There was absence of normal bradycardia following Valsalva maneuver in hypothyroid cases suggesting a reduced vagal reflex activity which might have resulted from the central cardiac vagal excitability due to low level of thyroid hormone in these patients. Valsalva ratio was less than 1.5 in hypothyroid patients; this also signifies altered vagal tone in hypothyroidism. In deep breath test 50% patients showed abnormal change in heart rate suggesting further reduced efferent vagal activity in study group. This observation supports the finding of Valsalva maneuver test.

Abnormal small rise of heart rate on standing in orthostatic test as observed in hypothyroid patients may be due to absence of abrupt reduction of cardiac vagal tone further suggesting modified vagal function. There was no significant fall of blood pressure after one minute of standing in orthostatic test. This indicates that sympathetic reflex arc is not much affected in hypothyroids.
Result of cold pressure test in hypothyroid patients was found to be comparable with that of control group indicating normal sympathetic tone in hypothyroid patients.

Handgrip test performed by the hypothyroid patients has shown similar result as found in cold pressor test. Thus the present study suggest that reflex vagal activity is altered without any change in sympathetic function in patients with hypothyroidism and thus Valsalva maneuver test, orthostatic test and deep breath test used in the present study may appear as useful tool for clinical diagnosis of hypothyroidism in areas lacking the modern diagnostic facilities. However more such trials should be undertaken in larger samples prior to employing these as diagnostic tools.

DISCUSSION: The thyroid hormone levels measured in the present study were found to be very much consistent with the other reports as well as the in accordance of clinical diagnosis. The clinical diagnosis of the hypothyroid patients included in the present study was so accurate that none of the patients diagnosed clinically as hypothyroid showed normal or otherwise inconsistent thyroid hormone levels. This is attributed to the strict protocol adopted for diagnosis of hypothyroid patients clinically during screening the patients in the OPD. Data obtained from the normal age and sex matched control subjects was also comparable with the data available in Indian & Western literature.

The mean Valsalva ratio in normal control subjects, an indicator of vagal reflex activity,

observed in the present study was 1.69 slightly more than 1.5 as reported by the Hutchinson[10] in 1989 & Levin[9] in 1966. However, the observations in the present study cannot be compared with the Levin study as the study group in the Levin study was much larger comprising of 200 patients as against in the present study where it was only 30. But the reflex bradycardia observed in hypothyroid patients was significantly reduced as compared to the control.

Kollai & Kollai[5] in 1988 have reported that depressed thyroid functions are associated with reduced vagal excitability suggesting the proposed central role of thyroid hormone in maintenance of vagal excitability. Iodothyronine has been shown to be present in different part of the central nervous system like medulla (Koizumi & Kollai[11] in 1981, Dratman[12] et al in 1982). Hypothalamus being the primary site for generation of vagal tone; this signifies the importance of thyroid hormone in the control mechanism of autonomic reflexes. Therefore it may be speculated that suppressed thyroid function associated with lower Valsalva ratio is due to central action of thyroid hormone on vagal tone.

The present study reveals that during orthostatic test heart rate rise in hypothyroid subjects immediately on standing was significantly lower as compared to normal subjects. This lower rise of heart rate observed in hypothyroid patients indicates blunt inhibition of vagal tone because it is known that immediate heart rate rise is a result of abrupt inhibition of cardiac vagal tone (Bannister[1] in 1988). The maximum/minimum heart rate ratio in control subject was 1.4 which is near to the value demonstrated by Bannister. However the mean ratio in hypothyroid patients being significantly less than control subject may be considered abnormal. This may appear physiological because the ratio in hypothyroid patients is still above 1.0, which has been considered normal in other studies (Bannister[1] in 1988a). The discrepancy between normal and study group may be due to wide variation in ratio found in normal population. The $30^{th}/15^{th}$ interval ratio in control and hypothyroid group was not found to be statistically significant in the present study which suggests that RR interval is not concluding evidence for the change in vagal activity in hypothyroid patients. The blood pressure change during supine posture as observed in the present study in hypothyroid patients was also insignificant as compared to normal subject. The systolic pressure & diastolic pressure was found in standing posture while no such changes were demonstrated by the hypothyroid patients hence it is difficult at his moment to conclude.

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