



Evaluation of Autonomic Functions in Hypothyroid Patients

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Abstract

Introduction: The clinical picture of hyperthyroidism is suggestive of increased sympathetic activity but assessments of sympathetic activity suggest that sympathetic outflow is either unchanged or reduced. In contrast, whereas several clinical features of hypothyroidism are consistent with reduced sympathetic activity, indirect techniques suggest that sympathetic activity is elevated. This study is conducted to understand the influence of hypothyroid conditions on autonomic functions.

Material and methods: Cross Sectional Study conducted on 62 patients who had already been diagnosed as hypothyroid, at the out-patient block.

Result and conclusion: E:I (Heart rate variability during deep and slow breathing) appears to be a more sensitive tool in detecting early autonomic changes than the other parameters. We observed a higher significant sympathetic response among the untreated hypothyroid group in comparison to the treated and control group.

Keywords: Autonomic Functions, Hypothyroid, sympathovagal, parasympathetic parameters, heart rate variability.

Introduction

Variations from euthyroid status affect virtually all physiological systems and effects on the cardiovascular system are particularly pronounced. Changes in thyroid status are associated with changes not only in cardiac and vascular function but are also believed to alter

autonomic regulation of cardiovascular system. The clinical picture of hyperthyroidism is suggestive of increased sympathetic activity but assessments of sympathetic activity suggest that sympathetic outflow is either unchanged or reduced. In contrast, whereas several clinical features of hypothyroidism are consistent with reduced sympathetic activity, indirect techniques suggest that sympathetic activity is elevated. Interestingly, in both hypothyroidism and hyperthyroidism- the influence of the parasympathetic nervous system on heart rate seems to be reduced. The autonomic nervous system commonly in co-operation with endocrine organ is called into action, involuntarily by acting on heart, smooth muscles and glands in such ways as will preserve the “fitness” of the internal environment for continued voluntary action. Constantly changing internal and external environmental stimuli triggered a multitude of adaptive adjustments in the functioning of the organs of the body reflexively through the neuronal network by modulating the sensory, visceral motor and neuro-endocrine functions. The mechanisms are rapid, dynamic and totally involuntary. Thyroid dysfunctions are common global health problems, hypothyroidism accounting for 5-15% and hyperthyroidism 0.3 to 0.6% in general population. Recently, the thyroid dysfunction has increased considerably and presently, the burden of thyroid disorders in India is about 42 million. It is not clearly known that the increased thyroid dysfunctions are directly linked with changes in the life style of the society. Thyroid hormones are the major regulating factors of body metabolism, and the degree of metabolism has a direct impact on sympathovagal balance. Thyroid dysfunctions are more common in

females compared to males; especially in hypothyroidism the male-female ratio is 1:6 to 8.

Hypothyroidism in general is a prominent hypometabolic state and sympathetic activities are anticipated to be less in this condition. It has been reported recently that hypothyroidism is associated with decreased sympathovagal modulations of cardiac activities. The patients with hypothyroidism often have autonomic neuropathies with a higher level of vagal tone that partly improves with thyroxine therapy, which suggest sympathovagal imbalance in hypothyroidism and its plausible link to the cardiovascular dysfunctions in the hypothyroidism.

Material and methodology: A cross sectional study, setting conducted by employing a battery of 5 (five) Autonomic Function Test in the research laboratory room having a quiet ambient temperature of 20°C to 23° C at the appointed day between 9a.m. to 4p.m. by multichannel polyrite. Taking 2% prevalence of hypothyroid disorders among the young population and with 5% significance levels, the sample size was calculated as 30. This study was conducted on 62(sixty two) hypothyroid patients, out of 62 hypothyroid patients 31 are treated and 31 are untreated hypothyroid patients. All patients with hypothyroid diagnosed on the basis of a detailed history, clinical stigmata of hypothyroid, thyroid profiles, out patients department (OPD) as well as endocrinology clinic. 31 healthy subjects served as control.

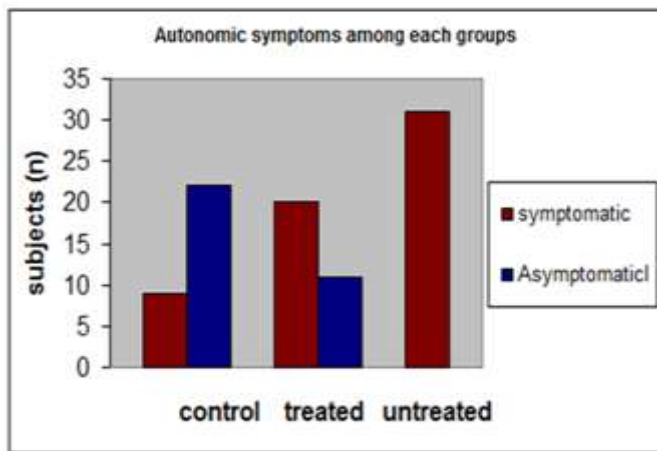
Exclusion Criteria

- Seriously ill patients.
- Patient with past or present clinical evidence of other associated diseases such as diabetes, hypertension, neurological deficits and renal impairment etc.
- Patient with habits such as alcoholism and smoking

Patient preparation: The patients were made to wear loose gowns and metallic objects like rings, watches etc were not allowed to wear. All the subjects were to rest for 15 minutes in supine position just before the commencement of the tests. The resting time after each test was 5 to 10 minutes.

- a. Baseline Cardiorespiratory Parameters: Heart Rate (HR), Systolic Blood Pressure (SBP) and Diastolic Blood Pressure(DBP).
- b. Parasympathetic Parameters:
 - Heart rate variability to deep and slow breathing (E:I)

Results:



Graph 1: Subjects with symptoms suggestive of autonomic dysfunction and those asymptomatic among the three groups. According to the responses from the questionnaire, only 9(29.3%) in the control, 20(64.52%) in the treated and 31(100%) in each group of 31 subjects complained of symptoms suggestive of autonomic dysfunction. The basal heart rate recorded among the groups were found within normal range. The difference in the means of these heart rates among the groups were found insignificant in all when tested by using student's t test.

Table 1: Basal heart rate recorded among the three groups. *All p values >0.05.

Sn.	Subjects (n= 31 in each group)	Mean ± SD	T value	P*
1	Control	70.16 ± 9.713	0.071	0.944
	Treated hypothyroidism	69.94 ± 14.9		
2	Untreated	74.71 ± 9.954	1.483	0.143
	treated	69.94± 14.9		
3	Control	70.16 ± 9.713	1.821	0.074
	Untreated hypothyroidism	74.71± 9.954		

Student's T test applied to test for significance in the difference of means of the basal systolic blood pressure between the three groups revealed that there was no significant difference between the control and the hypothyroidism treated groups, whereas between control and untreated and between treated and untreated, the untreated hypothyroidism group have their systolic blood pressure significantly higher than both control and untreated (Table.3).

Table 2: Comparison of the basal systolic blood pressure among the study groups *p values are <0.05

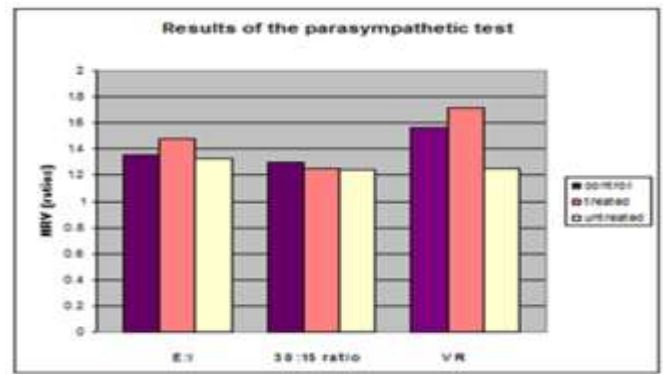
Sn.	Subjects (n= 31 in each group)	Mean ± SD	T value	p
1	Control	113.29± 14.213	1.553	0.126
	Treated hypothyroidism	118.52± 12.198		
2	Untreated hypothyroidism	126.61± 14.601	1.483	0.021*
	treated hypothyroidism	118.52± 12.198		
3	Control	113.29± 14.213	3.640	0.001*
	Untreated hypothyroidism	126.61± 14.601		

But after testing statistically using student’s t test in the difference of means of the basal diastolic blood pressure between groups, it was found that there was no significant difference in the diastolic blood pressure among the study groups from each other (Table 4).

Table 3: Comparison of the basal diastolic blood pressure (BDBP) among the study groups

Sn.	Subjects (n= 31 in each group)	Mean ± SD BDBP	T value	p
1	Control	75.48 ± 9.077	1.085	0.296
	Treated hypothyroidism	78.06 ± 10.152		
2	Untreated hypothyroidism	75.48 ± 9.371	0.715	0.477
	treated hypothyroidism	78.06 ± 10.152		
3	Control	75.48 ± 9.077	3.859	0.068
	Untreated hypothyroidism	75.48 ± 9.371		

The mean of the test results of the three parameters of parasympathetic integrity in the three groups (Fig. 5), when tested inter group wise by applying student’s t test we observed (1) In the E:I ratio, no difference between control and treated group, but untreated group showed significantly a poorer functioning comparing to treated group and as well as to control (Table 5). (2) In the 30:15 ratio, the result showed no significant difference from each other among the groups (Table 6). And (3) in the VR results, there was no difference between control and treated, but the untreated hypothyroidism group showed significantly lower abnormal values compared to control and treated groups (Table 7)



Graph 2: Mean in each of the three parasympathetic test parameters’ result among the three groups of subjects

Table 4: Comparison of the E:I ratio results among the study groups.*p =significant

Sn.	Subjects (n= 31 in each group)	Mean ± SD E:I	t value	p
1	Control	1.362 ± 0.167	2.903	0.005*
	Untreated hypothyroidism	1.326 ± 0.193		
2	Treated hypothyroidism	1.479 ± 0.147	3.496	0.001*
	Untreated hypothyroidism	1.326 ± 0.193		
3	Control	1.362 ± 0.167	0.793	0.431
	Treated hypothyroidism	1.479 ± 0.147		

Table 5: Comparison of the 30:15 ratio results among the study groups (p>0.05)

Sn.	Subjects (n= 31 in each group)	Mean ± SD 30:15	t value	p
1	Control	1.301 ± 0.293	0.910	0.367
	Treated hypothyroidism	1.247 ± 0.142		
2	Untreated hypothyroidism	1.243± 0.111	0.159	0.874
	treated hypothyroidism	1.247 ± 0.142		

3	Control	1.301 ± 0.293	1.037	0.304
	Untreated hypothyroidism	1.243± 0.111		

Table 6: The overall autonomic function test result after computing from the results of parasympathetic and sympathetic functions.

Sn.	Autonomic function severity	Control (n=31)	Hypothyroidism Treated (n=31)	Hypothyroidism untreated (n=31)
1	Normal	30 (96.77%)	14 (45.16%)	10(32.25%)
2	Early involvement	1(3.22%)	11 (35.48%)	16(51.61%)
3	Definitely	0	1(3.22%)	2(6.45%)
4	Severe	0	5 (16.12%)	3 (9.67%)
5	Atypical	0	0	0

Discussion

Thyroid dysfunction are common global health problems, hypothyroidism accounting for 5-15% in general population. If autonomic dysfunction can be detected early in hypothyroidism patient, invasive treatment could be planned to prevention or progress to severe involvement. Equivocal and conflicting reports of sympathetic and parasympathetic abnormalities are reported in various literatures like Xing H22 et al, Kahaly GJ et al. The results of the study benefit the patients in preventing complications arising out of autonomic dysfunction. Explanation of the autonomic characteristics of patients with hypothyroidism compared with healthy controls would also help determine whether any correlation exists between the autonomic profile, thyroid profile, lipid profile and clinical status of the patients vis-a-vis healthy controls. Kahaly GJ et al found that reduced heart rate variability or parasympathetic activity in treated hypothyroidism and Varonych SM et al also found in treated hypothyroid patients reduced parasympathetic activity. In contrary to our findings, Bhat AN et al. found no change in parasympathetic activity in hypothyroidism as well as

hyperthyroidism. In our study, E:I (Heart rate variability during deep and slow breathing) appears to be a more sensitive tool in detecting early autonomic changes than the other parameters. This has also been stated by Bannister et al (1999) and Ewing DJ et al. The significant difference between E:I levels between control, treated and untreated hypothyroid patients (P<0.05). They found that untreated group have lesser E:I value in comparison to treated and control groups i.e. parasympathetic activity which are decreased in untreated hypothyroid patients. Similar finding can be observed in the Inukai T et al, Inullai T et al. They have comment that in treated hypothyroidism parasympathetic activity may be improved. Other contrary findings are found in Heemstraw KA et al. Makusheva MV et al and Xing H et al. There are autonomic dysfunction in hypothyroidism. The loss of variability in autonomic control system has recently been linked with a number of cardiovascular diseases and dysfunction, particularly coronary heart diseases, myocardial infarction and cardiac arrhythmias which can be potentially fatal. Gautam S et al Kahaly GJ et al. are found similar result to our study. But in contrast to results of our study that

parasympathetic activity increased in untreated hypothyroidism found in Heemstraw KA et al. Makusheva MV et al and Xing H et al. Again Bhat AN et al give a totally different results that no changes of parasympathetic activity in hypothyroidism. Fommei E et al. found in untreated hypothyroidism in their study had increased blood pressure with increased activation of adrenergic system and they also found with significant reduction in basal BP in treated hypothyroidism. In our study also we found the SBP during PCT or SBP response on lying to standing significantly high at the end of 1 minute standing which reflect and increased sympathetic activity in untreated hypothyroidism. Also, in our study we observed a higher significant sympathetic response among the untreated hypothyroid group in comparison to the treated and control group. The result of the present study is different from Mahajan AS et al. who found no changes in SBP as well as DBP in both treated and untreated hypothyroidism. Our study shows DBP is significantly increase in all 3 groups during HGT at 4 minute.

Conclusion

Among the thyroid disorders, hypothyroidism occur in 05-15% of general population. Hypothyroidism is more common in females as compared to males. Hypothyroidism is linked significantly with autonomic dysfunction. The resultant autonomic dysfunction can result in various forms of cardiovascular disease such as coronary heart diseases, myocardial infarction and even cardiac arrhythmias. The traditional 5 Ewing's classical test (recommended by San Antonio Concession, 1988) is a reliable and well acceptable test for testing autonomic function in any clinical settings. Among the thyroid disorders, hypothyroidism is found to be associated with decreased cardiac-vagal tone (parasympathetic activity)

and increased sympathetic activity as found in our study. The highest number of treated as well as untreated hypothyroidism patients having autonomic nervous system dysfunction is of the early involvement pattern followed by severe pattern and least is definitely involved. Autonomic symptoms are appear to be more common among the female patients in comparison to their male counterpart.

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