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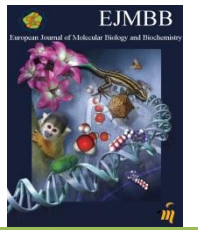

A STUDY ON CORRELATION BETWEEN SMOKING AND THYROID FUNCTION

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ABSTRACT

Background & Objectives: This study was conducted to explore possible correlation between smoking habit and thyroid hormone levels and function in Osmania general hospital, Hyderabad. A total of 82 volunteers i.e. all case were male screened. The effect of smoking on thyroid is believed to be due to the compound thiocyanate, a potent inhibitor of iodide transport, potentially capable of affecting the thyroid function. The aim of this study is to evaluate the thyroid hormones status in smokers. Methods: A case control study is done with 82 patients divided into 2 groups. Group 1 (healthy male non-smokers) as control and Group 2 (healthy male smokers) as cases with inclusion and exclusion criteria. Fasting blood samples were collected and serum TSH, T3 and T4 were measured. The data was analyzed using unpaired t test. Results: In the present study significant increase in thyroid hormones T3 and T4 levels is observed in the cases compared to the controls. Mean±S.D of T3 and T4 in Group 1 is 1.077±0.3469, 8.745±1.215 and in Group 2 is 1.541±0.3644, 9.822±2.066 respectively, there is a significant increase in the thyroid hormones of group 2. There is a significant decrease is serum TSH levels is observed in the cases compared to the controls. Mean±S.D of TSH in Group 1 is 2.712±0.8386 and Group 2 is 1.003±1.123, there is a significant decrease in serum TSH levels in Group 2. Interpretations & Conclusion: The findings in this study indicates that smoking is associated with biochemical hyperthyroidism. Hence evaluating thyroid hormone status in smokers might help in identifying occurrence of thyroid disorders and appropriate measures could be taken to prevent severity of morbidity and mortality associated with smoking.

INTRODUCTION

Cigarettes are considered as the commonest source of toxic chemical exposure and chemically mediated illness in humans. Globally, tobacco use is one of the commonest licit substances of abuse and is projected to kill 50% more people than HIV/AIDS by 2015, and to be responsible for 10% of all deaths by 2030. Of great concern is the fact that more than 80% of these deaths are expected to occur in low and middle income countries including India [1]. The first Global Adult Tobacco Survey of 2010 reports that currently 34.6%of adults (47.9% males and 20.3% females)\ in India are users of tobacco products.[2] Additionally, prevalence of tobacco use is high among people seeking help for use of other psychoactive substances as well [3]. In view of the magnitude of the problem, it becomes necessary for us to understand the effect of tobacco on various body systems.

Tobacco smoke contains substances that affect the function of the thyroid. Studies show that smokers are more likely to have thyroid enlargement, and it is possible that mild thyroid enlargement in smokers could be a sign of subtle thyroid disturbance. According to a previous

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study smokers are twice as likely as non-smokers to develop Graves' disease. Smoking also apparently worsens eye problems in people with Graves' disease. Smoking may increase the risk of hypothyroidism in patients with Hashimoto's thyroiditis. The effects of smoking on the of endocrine glands function have been investigated. It is revealed that the most component of smoke, produced from tobacco, has effects on the endocrine system is nicotine [4-6]. The present study aimed to study a possible association between smoking habit and thyroid volume and function.

Materials and methods

Settings: A case control study was conducted in the Department of Biochemistry, Osmania General Hospital, Hyderabad.

Sources of samples and data: The cases and samples were collected from Department of General Medicine, Osmania General Hospital, Afzalgunj and Department of Biochemistry, Osmania General Hospital.

Cases: Healthy male smokers, a brief history was taken and samples were collected.

Investigations were performed at the Department of Biochemistry, Osmania Medical College / Osmania General Hospital.

Controls

Healthy male non-smokers, a brief history was taken and samples were collected and investigations were performed at the Department of Biochemistry, Osmania Medical College / Osmania General Hospital.

In the present study the individuals were divided into two groups.

Group 1	Healthy male non - smokers	N = 41
Group 2	Healthy male smokers	N = 41

Informed oral and written consent was taken from all individuals who took part in the study.

Inclusion criteria

1) Smokers 2) No history of thyroid disease 3) Healthy males 4) No history of any steroids medication 5) No history of liver disease 6) Age between 25 to 50 years 7) No pituitary disorders.

Exclusion criteria

1) Non – smokers 2) History of thyroid disease 3) History of consumption of steroids medication 4) History of liver disease 6) Age less than 25 years and above 50 years 7) Patients with pituitary disorder

SPECIMEN COLLECTION

4ml of Fasting venous blood were collected in a vacutainer (RED CAP). Sample was centrifuged at 3000 r.p.m for 10 minutes and serum was separated for analysis within two hours of collection of blood. Grossly haemolysed and lipemic samples were excluded.

Parameters estimated

1) Serum TSH
2) Serum total T_3 (TT_3)
3) Serum total T_4 (TT_4)

The ethical issues involved in this study were reviewed and approved by the ethics scientific committee of Osmania Medical College.

STATISTICS ANALYSIS: The data was analysed using GraphPad prism 6.0

Methodology

TSH (Thyroid stimulating hormone), T3 and T4 estimated by Method: ELISA (CALBIOTECH KIT) – TS227T [7].

Results

In the present study, a total of 82 cases were analyzed. We divided into two groups, that is smokers and non-smokers. Non-smokers had all the three parameters that is TSH, T3 and T4 within normal limits.

In this study we analyzed data on 82 men, of whom 41 were smokers and 41 were non-smokers. In this study the age range for the study population was 25 to 48 years. The minimum age is 25.00 years, median age is 31.50 years and the maximum age is 48.00 years of the total study population respectively.

The numbers of cigarettes smoked in a smoking population is minimum 3 per day and maximum 40 per day and the duration of smoking was minimum of 3 years and maximum of 25 years. In this study the Mean ± SD of TSH was lower for smokers than non-smoker. The mean and median of TSH value in this study population is 1.857 and 1.940 respectively.

Among 41 smokers (Group 2) 24 cases were positive for abnormally low TSH with a percentage of 58.54% (95% CI 42.11 – 73.68%) and is statistically significant. In the present study, 41 smokers (Group 2) 8 cases were positive for abnormally high T3 with a percentage of 19.51% (95% CI 8.82 – 34.87%) and is statistically significant. The total study population, among 41 smokers (Group 2) 19 cases were positive for abnormally high T4 with a percentage of 46.34% (95% CI 3.662 – 62.53%) and is statistically significant.

Table 1: Mean ± SD of studied parameters in all groups

Parameter	Group 1 (control)			Group 2 (CASES)		
	Mean	±S.D	SEM	Mean	±S.D	SEM
TSH*	2.712	0.8386	0.1310	1.003	1.123	0.1754
T3*	1.077	0.3469	0.05418	1.541	0.3644	0.05691
T4*	8.745	1.215	0.1898	9.822	2.066	0.3226

Association of smoking with abnormal thyroid levels between 2 groups

Table 2: **Association of smoking with abnormal TSH between Group 1(n = 41) and Group 2 (n = 41)**

	Positive	Negative
Group 1	0	41
Group 2	17	24

Table 3: Association of smoking with abnormal T3 between Group 1 (n = 41) and Group 2 (n = 41)

	Positive	Negative
Group 1	0	41
Group 2	8	33

Table 4: Association of smoking with abnormal T4 between Group 1 (n = 41) and Group 2 (n = 41)

	Positive	Negative
Group 1	0	41
Group 2	19	22

Table 5: Positive thyroid abnormal results in total study population (N = 82)

	No. of cases	Percentage %	95% Confidence interval
TSH Abnormal	24	58.54	42.11 – 73.68
T3 Abnormal	8	19.51	8.82 – 34.87
T4 Abnormal	19	46.34	3.662 – 62.53

Table 6: Abnormal thyroid Results among smoker population

	No. of Positive cases	Percentage %	95% Confidence interval
TSH Abnormal	24	58.54	42.11 – 73.68
T3 Abnormal	8	19.51	8.82 – 34.87
T4 Abnormal	19	46.34	3.662 – 62.53

DISCUSSION

The thyroid gland controls almost all of the metabolic processes in the body. The most common thyroid disorder involves abnormal production of thyroid hormones. Hyperthyroidism means too much of thyroid hormone, on the other hand, insufficient hormone production leads to hypothyroidism.

In a study done by Christensen et al, smokers were found to have TSH levels insignificantly lower in smokers than in non-smokers [8]. A possible mechanism could be enhanced activity of the hepatic oxidative system, induced by benzpyrene in smoke. Lower levels of TSH among smokers have generally been reported in most studies [9].

A study by Chester L Fisher et al, found that current smokers have lower TSH levels than never smokers and former smokers and concluded that these findings are probably related to higher levels thyroxine-binding globulin, testosterone and other toxicological mechanisms. They also suggested that in smokers with normal clinical examination suppressed TSH levels may represent a smoking effect and not intrinsic thyroid disease [9].

A study by Soldin P et al, suggested that active and passive smoking was associated with a higher risk of having a significantly lower TSH levels compared to non-smokers, suggesting that there was an inhibitory effect of cigarette smoke exposure on the thyroid.

Belin et al in the Third National Health and Nutrition Examination Survey (NHANES III), found that fewer smokers had elevated TSH levels compared with non-smokers and concluded that smoking is associated with less development of thyroid autoantibodies and more prevalent TSH elevation [11]. Their data was consistent with the hypothesis that decreased thyroid iodide transport and organification in smokers protect against development of autoantibodies, but predispose iodine-deficient individuals to hypothyroidism.

In contrary to our study L. Hegedus et al found slight difference in serum TSH level between smokers and non-smokers which probably had no physiopathological significance [12].

In the present study, the Mean ± SD of serum T4 levels in Group 1 was 8.745 ± 1.215 and group 2 was 9.822 ± 2.066. The increase in serum T4 levels in group 2 was significant ($p < 0.0051$). This implied that smokers have abnormally high serum T4 levels when compared to controls. Due to certain environmental toxins and cigarette smoke which can significantly increase SCN− concentrations to levels potentially capable of affecting the thyroid gland. Thiocyanate [SCN^-] inhibits iodide transport and organification as well as increases the release of iodide from the thyroid. Thiocyanite [SCN^-] can cause goiter in iodine deficiency, while 2-3hydroxypyridine, a tobacco smoke toxin, inhibits thyroxin deiodination by reducing iodothyronin doiodenase activity. This temporary effect mildly elevates serum thyroxin levels due to its deiodenase altering activity.

These findings were in concordance with the following studies. Study conducted by Chester L fisher et al showed significantly higher serum T4 levels among current smokers than among former smokers and never smokers [9]. Increase in T4 was thought to be related to a decrease in thyroid-binding globulin that was associated with androgen therapy. They also stated that tobacco smoke constituent, 2,3-hydroxypyridine may slightly and temporarily elevate serum T4 levels as a consequence of its deiodinase altering activity prior to decreasing these levels

and Hydroxyquinones, also found in tobacco smoke, increase intracellular calcium and cause hepatotoxicity [13]. This disruption could impair degradation of T4 resulting in elevated serum levels.

In contrary to our study Sepkovic et al observed lower (P< .05) serum T4 levels in heavy smokers than those of nonsmokers. They explained Thiocyanate, present in tobacco smoke has a molecular size quite close to that of iodide [14]. It also demonstrates antithyroid activity where it has been extensively used to block the reuptake of iodide by the thyroid. Thiocyanate alters the iodine pump by inhibiting the oxidation of iodine and by inhibiting tyrosine iodination effects that could lower circulating hormone levels [15].

In a study by Melander A et al, stated that influence of smoking on T4 turnover is not likely to be inhibitory, as smoking stimulates rather than inhibits hepatic oxidative metabolism and suggested that smoking may promote a modestly increased secretion of thyroid hormone that normalizes after leaving off smoking [16]. Thus assumed smoking-induced increase in thyroid hormone secretion is secretion by is due to enhanced sympathetic nervous activity.

In the present study we compared the Mean ± SD of serum T3 levels in Group 1 was 1.077 ± 0.3469 and Group 2 was 1.541 ± 0.3644. The increase in serum T3 levels in Group 2 was significant ($p < 0.0001$). This implied that smokers have higher serum T3 levels compared to controls. It can be assumed that the increase in T3 levels was resulting from either enhanced production or reduced clearance. A constituent of tobacco smoke, benzpyrene is known to induce hepatic conversion of T4 to T3 which is stimulated due to hepatic oxidative metabolism.

A study done by Karakaya A et al, also observed high serum T3 levels in heavy smokers than those of non-smokers [17]. This, finding supports the view that smoking can stimulate the extra thyroidal conversion of T4 to T3. A possible mechanism could be enhanced activity of the hepatic oxidative system, induced by benzpyrene in smoke [18].

This was similar to study by Christensen SB et al. They found higher serum T3 levels in heavy smokers than never smokers. It can be assumed that the increase in T3 was resulting from either enhanced production or reduced clearance [8]. This finding emphasizes the possibility that there are both transient and sustained effects of smoking and cessation of smoking on thyroid hormone economy.

Thus several mechanisms have been postulated to show the effect of smoking on thyroid hormones. This may be due to increased thyroid autonomy caused by the iodine depletion of the thyroid by SCN−. However, nicotine-dependent stimulation of the sympathetic nervous system, which in turn stimulates the thyroid gland and enhances the secretion of thyroid hormones, might also be responsible for the lower TSH levels in smokers. Another constituent of smoke, benzpyrene, is known to stimulate hepatic oxidative metabolism, which in turn may stimulate hepatic conversion of T4 to T3 [18].

Thiocyanate in cigarette smoke has inhibitory effects on the synthesis of thyroid hormones by inhibiting the uptake and organification of iodide [19.

Nicotine present in tobacco smoke stimulates the sympathetic nervous system, which in turn stimulates the thyroid gland and enhances the secretion of thyroid hormones. Another constituent of smoke, Benzpyrene, is known to stimulate hepatic oxidative metabolism which in turn may have stimulatory effect on thyroid hormone synthesis [20].

A correct interpretation of the modification of serum TSH, T3 and T4 concentration is crucial to correctly asses the alteration in thyroid function in smokers. In the present study there is decrease in TSH levels with increase in T3 and T4 levels in male smokers with non-smokers. These findings indicate that there is a state of biochemical hyperthyroidism in smokers as compared to non-smokers.

In addition to TSH, T3 and T4 for predicting thyroid disorders in smokers, other biomarker such as thyroid peroxidase antibody (TPO-Ab) thyroglobulin antibody (Tg-Ab) and thiocyanate (SCN^-) can be used for predicting thyroid disorder in smokers.

CONCLUSION

Tobacco smoking modifies almost all functions of the thyroid gland. Currently, studies point toward a robust association between smoking and Graves' disease and in particular Grave's orbitopathy. Additionally, two interesting findings of decrease risk of Hashimoto's thyroiditis and thyroid cancer require further elaboration and clinical judgement if the benefits can outweigh the numerous toxic and detrimental effect of tobacco smoke on the human physiological system.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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