Does smoking affect thyroid gland enlargement and nodule formation in iodine-sufficient regions?

Le tabagisme a-t-il un effet sur la formation du goitre et des nodules thyroïdiens dans les régions où l'apport en iode est suffisant?

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Abstract

Objectives. – The present study aimed to investigate the effect of smoking on thyroid nodule formation and goiter development in healthy subjects living in Istanbul, an iodine-sufficient region. This study was designed as a prospective, randomized, and observational study. Methods. – Included in the study were voluntary hospital staff and relatives of patients between the ages of 28 and 71 who had no known disease or drug use, who have been living in Istanbul and had been smoking more than 10 cigarettes per day for at least 10 years. Nonsmoker volunteers (45) shared similar demographic characteristics and were matched for age to the (46) smokers. By means of thyroid ultrasounds performed in all participants, volumes of the right and left lobes of the thyroid gland, and number, diameter and characteristics of nodules were evaluated. Results. – Comparing the smokers and nonsmokers, no statistically significant difference was determined in terms of presence of nodules and volumes of the left and right thyroid lobes (P = 0.68, P = 0.09, and P = 0.63, respectively). Making enhanced diffuse enlargement of the thyroid gland, but not to a statistically significant degree. Smoking was observed to have no effect on non-toxic nodules, or the levels of thyroid-stimulating hormone, free thyroxin, free triiodothyronine, anti-thyroid peroxidase, or anti-thyroglobulin antibodies. Conclusions. – Smoking does not effect, to a statistically significant degree goiter development thyroid nodule formation in iodine-sufficient regions like Istanbul.

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Résumé

L’objectif de cette étude était d’examiner l’effet du tabagisme sur la formation des nodules thyroïdiens et du goitre chez des sujets sains habitant à Istanbul, une région où l’apport en iode est suffisant. Il s’agit d’une étude observationnelle prospective et randomisée. Les volontaires fumeurs recrutés parmi les équipes hospitalières et les proches de patients étaient âgés de 28 à 71 ans, ne présentaient pas de maladie connue et ne prenaient pas de médicaments, résidaient à Istanbul et fumaient plus de dix cigarettes par jour depuis au moins dix ans. Les volontaires non fumeurs (n = 45) présentant les mêmes caractéristiques démographiques étaient appariés par l’âge aux volontaires fumeurs (n = 46). Une échographie thyroïdienne était réalisée chez tous les sujets afin de mesurer les volumes des lobes droite et gauche et le nombre, diamètre et caractéristiques des nodules observés. La comparaison entre les fumeurs et non-fumeurs ne montrait pas de différence significative en ce qui concerne la présence de nodules et les volumes des lobes glandulaires (respectivement p = 0,68 ; p = 0,09 ; p = 0,63). Le tabagisme favorise le grossissement diffus de la glande thyroïdienne, mais sans atteindre le niveau de signification statistique. Il n’a pas d’effet sur les nodules non toxiques, ni sur les taux de TSH, de thyroxine libre, de triiodothyronine libre, de peroxydase antithyroïdienne ou des anticorps antithyroglobulines. En conclusion, le tabagisme n’a pas d’effet statistiquement significatif sur la formation de goitre ni de nodules thyroïdiens dans des régions comme Istanbul où l’apport en iode est suffisant.

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1. Introduction

The association of tobacco smoking with thyroid enlargement and nodule formation remains a matter of debate. Numerous factors are known to play a role in diffuse and nodular enlargement of the thyroid gland. Generally, these factors include thyroid-stimulating hormone (TSH) level, iodine concentration, thyroid autoantibodies, and foods and drinking water that contain goitrogens. However, the effect of gender, age, body weight, or personal habits such as smoking and alcohol consumption on thyroid volume is controversial. Some previous studies have identified a strong association between smoking and goiter in iodine-deficient regions. Some experimental studies have shown that thiocyanate, a major component of smoke derived from hydrogen cyanide, is the mediator of the goitrogenic effect of tobacco smoke acting as a competitive inhibitor of iodine uptake. It is thought that the above-mentioned effects of smoking are further increased in iodine-deficient regions, and thereby cause thyroid gland enlargement. However, to our knowledge, only a limited number of studies have investigated the relationship of smoking with nodule and goiter in iodine-sufficient regions, and the reported results are contradictory [1–9]. The present study aimed to investigate the effect of smoking on thyroid nodule formation and goiter development in healthy subjects who have been living in Istanbul, an iodine-sufficient region.

2. Patients and methods

2.1. Study design and patients

The present study, designed as a prospective, randomized, and observational study, was conducted between January and June 2011 in the Internal Medicine Clinic of Haydarpasa Numune Training and Research Hospital. The study protocol was in accordance with the Declaration of Helsinki and was approved by the Hospital Ethics Committee, and consent forms were obtained from all participants. Voluntary hospital staff and relatives of patients who had no known disease or drug use and who had been living in Istanbul and smoking at least 10 cigarettes per day for at least 10 years were included in the study. Volunteers who were never smoked are accepted to nonsmoker group. Study involved patients those were born in Istanbul or patients who were born in places near to Istanbul that iodine deficiency was not frequent (Bursa, Canakkale, Edirne, etc.) and moved to Istanbul before the age of 10 years old. The nonsmoker volunteers had similar demographic characteristics to the smokers and were matched for age.

2.2. Ultrasound

Thyroid ultrasound (US) was performed on all participants by one radiologist who was blinded as to the groups. The subjects were examined in the supine position with the head in mild hyperextension. Thyroid US was performed using a Toshiba Aplio XV (SSA-770-32) US device United States, California with a 7.5 MHz linear transducer-probe. The gray scale US features were used. Volume was calculated by measuring the three dimensions of first the right lobe and then the left lobe. The volume for each lobe was calculated using the following formula: length × width × depth × 0.479 (mL) [10]. The size of the isthmus was determined by measuring only its anteroposterior (AP) diameter. Characteristics and sizes of any nodules detected in the thyroid gland were determined. After examination of the thyroid gland, both sides of the neck were examined and pathological findings were reported. To avoid variation of USG operators in repeating measurements, axises of the istmus and thyroid gland are measured by the widest section in an AP transverse section. These measurements are the ones in which the least variation was observed between different USG operators.

2.3. Blood test

Blood samples were obtained between 8:00 and 9:00 am after 12 hours of fasting. These were analyzed on the same day for TSH, free thyroxine (FT4), anti-thyroid peroxidase (anti-TPO) antibodies, as well as anti-thyroglobulin (anti-Tg) antibody levels. The levels of TSH, FT4, FT3, as well as anti-TPO and anti-Tg antibodies were measured using a chemiluminescent immunoassay (DPC, USA). The normal reference ranges were 0.34 to 5.6 μIU/mL for TSH, 0.58 to 1.64 ng/dL for FT4, 2.3 to 3.9 pg/mL for FT3, less than 9 IU/mL for anti-TPO antibody, and 0.9 to 4.0 IU/mL for anti-Tg antibody. Targeted coefficient of variation (CV) levels was less than 10% for TSH, less than 10% for FT3, less than 10% for FT4, less than 10% for TSH according to Clinical and Laboratory Standards Institute (CLSI). TSH, FT4 and FT3 were worked in 80 samples to find the CV value of kit, which was used for these parameters. The highest value was 5.3% for TSH, 5.0% for FT3, 7.8% for FT4.

Systemic examination was performed on all subjects by an endocrinologist; body weight and height were measured, and body mass index (BMI) was calculated using the following formula: BMI = body weight (kg)/[height (m)]².

2.4. Statistical analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA) version 13.0. In addition to descriptive statistics (mean, median, and standard deviation), a t-test was performed for the comparison of normally distributed data, and the Mann-Whitney U test was used to compare the non-normally distributed data. Proportional data were compared using the chi-square test. A two-sided P value <0.05 was considered statistically significant.

3. Results

Included in the present study were 91 participants (46 smokers, 45 non-smokers), but then nine were excluded due to the presence of various thyroid diseases (Fig. 1). Ages of the 91 participants ranged from 28 to 71 and mean age 42.7 ± 10 years. No statistically significant difference was found between the smokers (21 males, 25 females) and nonsmokers (15 males, 30 females) in terms of gender distribution (P = 0.23) nor...
Laboratory results of the study participants.

**Table 1**

<table>
<thead>
<tr>
<th></th>
<th>Smokers</th>
<th>Non-smokers</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 46)</td>
<td>(n = 45)</td>
<td></td>
</tr>
<tr>
<td>Nodule</td>
<td></td>
<td></td>
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<tr>
<td>Present (n (%))</td>
<td>13 (28.3)</td>
<td>11 (24.4)</td>
<td>0.68</td>
</tr>
<tr>
<td>Absent (n (%))</td>
<td>33 (71.7)</td>
<td>34 (75.6)</td>
<td></td>
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<tr>
<td>Right thyroid lobe volume (mL) (mean ± sd)</td>
<td>6.72 ± 2.5</td>
<td>5.96 ± 1.6</td>
<td>0.09</td>
</tr>
<tr>
<td>Left thyroid lobe volume (mL) (mean ± sd)</td>
<td>6.47 ± 2.7</td>
<td>6.21 ± 2.54</td>
<td>0.63</td>
</tr>
</tbody>
</table>

Data are presented n (%) or mean ± standard deviation (mean ± sd), where appropriate.

4. Discussion

The present study was performed on healthy subjects with no known disease who have been living in Istanbul, an iodine-sufficient region. It was determined that smoking has no effect on thyroid hormone levels, autoantibody development, or the size and shape of the thyroid gland.

Smoking influences various metabolic and biologic processes, as well as hormone secretion, in the human body. The causes of thyroid diseases, non-toxic goiter, nodule formation, and the associated preventive measures remain unclear. It is noteworthy that goiter development is more frequent in iodine-deficient regions. Although the frequency of a goiter rapidly decreases with iodine supplementation, the goiter itself cannot be completely eradicated, thereby highlighting that various other etiological factors might influence goiter development and nodule formation. In this context, smoking has attracted attention. The finding of an enlarged thyroid gland among smokers, particularly in the iodine-deficient regions, is of importance. Nevertheless, the association of smoking with diffuse and nodular enlargement of the thyroid gland has not been adequately investigated in iodine-sufficient regions [11,12]. Nicotine, a main component of cigarettes, is known to not affect iodine metabolism in the thyroid gland; however, its effect on hormone secretion from the thyroid gland is unknown. Colzani et al. [13] intravenously administered high-dose nicotine (equivalent to smoking two packs per day) to their study rats for 7 days in order to investigate the effects of nicotine on thyroid function. They reported that nicotine had no effect on thyroid function (T3, T4, and TSH levels), thyroid weight, or hormone synthesis and metabolism [13].

In a meta-analysis examining the results of three studies, an association between goiter and smoking was reported in iodine-deficient regions [14,15]. In a study from Sweden, smoking was reported to be associated with goiter and non-toxic thyroid nodules, an association found to be stronger in areas of endemic iodine deficiency [16]. In a study conducted in Turkey, the patients were divided into three groups according to their urinary iodine excretion levels, and the rate of smoking was found to be higher in the group with iodine deficiency [11]. Lio et al. [17] investigated women with goiter in three groups and found no association between the size of goiter and smoking.

We found a (not statistically significant) increase in the thyroid volume among the smokers when compared to the nonsmokers, and no statistically significant difference was identified in terms of the frequency of nodules. Despite the reported association between smoking and goiter in iodine-deficient regions, the lack of a difference in the iodine-sufficient regions supports the results of the present study [6,11–16].

Limitation of the study, the number of subjects in the present study may be inadequate to draw a conclusion about Istanbul’s general population; however, the likelihood of margin of error was decreased because the demographic characteristics of the two groups were similar except for smoking.
not statistically significant, females outnumbered males, particularly in the nonsmoker group. Nonsmokers were found to have higher (although not statistically significant) BMI values. Previous studies have shown that thyroid volume increases with increasing BMI [16], but in the present study, while the BMI values were lower in the smokers, thyroid volumes were higher than in nonsmokers. Still, the difference did not achieve statistical significance.

In conclusion, smoking enhanced diffuse enlargement of the thyroid gland, although not to a statistically significant degree. However, smoking was noted to have no effect on non-toxic nodules nor on TSH, FT4, FT3, or anti-TPO and anti-Tg antibodies. Thus, it can be stated that smoking does not influence goiter and thyroid nodule development in iodine-sufficient regions like Istanbul. Further large-scale studies are required to clarify the effect of smoking on thyroid gland enlargement and nodule formation.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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References