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SNORING, SYMPATHETIC ACTIVITY AND CARDIOVASCULAR RISK FACTORS IN A 70 YEAR OLD POPULATION

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In order to describe the relation between snoring, cardiovascular risk factors, metabolic factors and sympathetitic activity, 804 70-year-old males and females were classified according to snoring habits and life-style factors (alcohol and tobacco consumption), blood pressure, body mass index (BMI), plasma lipids (triglycerides, cholesterol, high density lipoprotein), plasma catecholamines (epinephrine, norepinephrine), fasting blood glucose and glucose tolerance test (1 gram glucose per kg body weight given and blood glucose was measured 1 and 2 hours thereafter) were evaluated in all participants.

Self-reported snoring was associated with gender (males showed higher prevalence than females, $p < 0.05$), alcohol consumption ($p < 0.01$), BMI ($p < 0.001$), systolic ($p < 0.01$) and diastolic ($p < 0.05$) blood pressure, glucose tolerance test ($p < 0.01$), plasma norepinephrine ($p < 0.05$) and partly with tobacco consumption ($p = 0.08$). No associations were found between snoring and fasting glucose, plasma lipids, plasma epinephrine or in the use of antihypertensive medication.

In multivariate analysis, with forced entry of gender, BMI, physical activity, alcohol and tobacco consumption, the relation between snoring and blood pressure ceased; only systolic blood pressure was associated with snoring ($p < 0.05$). Snoring was still associated with plasma norepinephrine ($p < 0.001$) and abnormal glucose tolerance ($p < 0.001$).

We conclude that, in a 70-year-old population, snoring is associated with gender, BMI and alcohol consumption. Snores showed higher plasma norepinephrine and abnormal glucose tolerance.

INTRODUCTION

Earlier epidemiologic studies have focussed upon an associated between every-night (habitual) snoring and cardiovascular/cerebrovascular morbidity and mortality (4, 14-18). The relations have been questioned, since validation of questionnaire information and controlling for the influence of potential confounders, e.g., body mass index (BMI), blood pressure, smoking and alcohol consumption, has been inadequate (25). When introducing BMI and life-style-variables the association between snoring and blood pressure ceases (10, 12). Different studies suggest that patients with sleep apnea may show changes in nocturnal metabolism and sympathetic activity (7-9). Since patients with sleep apnea in general are snorers (11, 27), we found it of interest to study whether or not snoring was associated with sympathetic activity and glucose metabolism. This issue has never been studied in an epidemiologic survey.

The aim of this study was to evaluate an elderly group of snorers cardiovascular risk profile including

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plasma lipids, plasma catecholamines and glucose metabolism.

SUBJECTS AND METHODS

The data used are derived from The Glostrup Population Studies. The study was initiated in 1964 as a prospective cardiovascular cohort study of 50 year olds born in 1914, and examined in 1974 (20). Approximately 20 years later, in 1984/1985, a new baseline was established (21).

All survivors were traced by means of the Danish Central Person Register and invited to take part in a clinical follow-up study. 1119 persons, all 70 years of age at the time of admission were selected. All were invited to a general health examination at the hospital. Eight hundred and four persons (72% - 392 men and 412 females) participated.

The 1984/85 study took at the Division of Prospective Medicine, Glostrup University Hospital. The examination was comprised of:

1. An interview based on a previously completed questionnaire.
2. A clinical examination including measurements of height, weight and blood pressure.
3. A fasting venous blood sample between 8 and 9 a.m. following a fasting period of a minimum 12 hours.

Questionnaire

Snoring habits: The question was phrased: "Do you know or have you been told that you snore during the night?". Answer options were 'never', 'rarely or hardly every', were 'sometimes' or 'always or almost always'. Those reporting 'always or almost always' were defined as snorers (habitual snorers), the rest as non-snorers.

Tobacco consumption: Smokers gave information on the number of cigarettes, cheroots, cigars and number of grams of pipe tobacco smoked/day, and their daily use of tobacco was estimated: one cigarette equalled one gram, one cheroot three grams and one cigar four grams of tobacco.

Alcohol consumption: Average daily alcohol consumption was calculated from the questionnaire. One beverage corresponded to approximately 10 grams of ethanol.

Physical activity: physical activity (any type of walking, bicycling, sports, etc.) in hours per week was noted.

Clinical examination

Blood pressure (BP): was measured twice, by the same nurse, on the right arm with the subject seated in a supine position, after a rest period of at least 10 minutes between 8 and 9 a.m. (19).

Body mass index (BMI): was calculated as weight in kilograms/height in squaremeters (kg/sqm).

Venous blood sample

Plasma epinephrine and norepinephrine were determined by a single isotope derivative technique (2).

High Density Lipoprotein (HDL), cholesterol and triglyceride: were determined (23).

Blood glucose: was determined and a *glucose tolerance test* was performed by the following: 1 g of glucose per kg body weight was given. Blood glucose was measured one and two hours after glucose ingestion.

Statistics

All data were analyzed by use of descriptive statistics, student t-test and chi-square test. In order to evaluate the influence of gender, BMI, physical activity alcohol and tobacco consumption a stepwise multiple regression analysis was performed. The influence of these potential confounders were evaluated using a stepwise multiple regression analysis with forced entry with snoring as a binary outcome variable. Probability-to-enter was for all analyses $p < 0.05$. A final analysis including all factors was performed using the same criteria.

The above analyses were carried out using the SPSSPC+ statistical software, version 3.1.

A p-value of < 0.05 was regarded as statistically significant for all analyses. All values are given as percent or mean (Standard Deviation - SD).

Ethics

The study was approved by the Copenhagen County Ethics Committee for Medical Research.

RESULTS

758 (94.2%) of the 804 persons answered the questions about snoring, 46 (5.8%) of the participants did not know whether they snored or not or did not give an answer to the question.

Snoring was reported by 46.2% of the males and 38.3% of the females ($p < 0.05$). Systolic blood pressure, pulse rate, blood glucose after 2 hours in the glucose tolerance test, total cholesterol and HDL-cholesterol were lower in males than females. Plasma epinephrine, alcohol and tobacco consumption were higher in males than females. No differences were found in diastolic blood pressure, plasma norepinephrine, fasting blood glucose, blood glucose after 1 hour in the glucose tolerance test, serum triglyceride, BMI, physical activity or daily use of

antihypertensive medication between males and females (Table 1).

In univariate analysis snorers showed higher systolic and diastolic blood pressure, plasma norepinephrine, glucose tolerance test after one and two hours, BMI and alcohol consumption. Tobacco consumption was slightly higher in snorers than non-snorers but this did not reach statistical significance ($p = 0.08$). No differences were found between plasma epinephrine, fasting blood glucose, total cholesterol, HDL-cholesterol, triglyceride, physical activity or daily use of antihypertensive medication between snorers and non-snorers (Table 2). In the multiple regression analysis, snoring was associated with systolic blood pressure, plasma norepinephrine, blood glucose after 1 and 2 hours, BMI, alcohol consumption and slightly to physical activity ($p = 0.09$).

TABLE 1. - Snoring, systolic and diastolic blood pressure (SBP and DBP), pulse rate, plasma norepinephrine and epinephrine, fasting blood glucose, glucose tolerance test (blood glucose and 1 and 2 hours after ingestion of 1 g glucose/kg body weight), fasting plasma lipids (total cholesterol, triglycerides, high density lipoprotein [HDL]) use of antihypertensive medication, body mass index (BMI), tobacco and alcohol consumption and physical activity in relation to gender, in a 70-year-old population.

	Males (SD)	Females (SD)	p*
Snoring	46.2%	38.3%	< 0.05
SBP (mmHg)	138.7 (19.9)	141.5 (19.4)	< 0.05
DBP (mmHg)	81.4 (10.4)	80.7 (10.6)	NS
Pulse rate (beats per minutes)	72.1 (11.1)	75.2 (11.0)	< 0.0001
Plasma Norepinephrine (ng/ml)	0.34 (0.14)	0.35 (0.13)	NS
Plasma Epinephrine (ng/ml)	0.031 (0.026)	0.023 (0.020)	< 0.0001
Fasting blood glucose (mmol/dl)	4.9 (1.5)	4.9 (1.7)	NS
Glucose, 1 hour (mmol/dl)	7.7 (2.1)	7.9 (2.3)	NS
Glucose, 2 hours (mmol/dl)	5.7 (2.4)	6.2 (2.4)	< 0.05
Cholesterol (mmol/dl)	6.2 (1.1)	7.0 (1.2)	< 0.0001
Tryglyceride (mmol/dl)	1.5 (0.8)	1.5 (0.8)	NS
HDL (mmol/dl)	1.3 (0.4)	1.6 (0.5)	< 0.0001
Daily use of antihypertensive medication	2.9%	5.6%	NS
BMI (kg/sqm)	25.2 (3.7)	25.5 (4.9)	NS
Tobacco consumption (g/day)	15.8 (14.2)	7.0 (9.1)	< 0.0001
Alcohol consumption	10.7 (12.2)	3.1 (5.3)	< 0.001
Physical activity (minutes per week)	51.3 (48.7)	48.9 (40.1)	NS

* t-test X^2 test.

TABLE 2. - Systolic and diastolic blood pressure (SBP and DBP), pulse rate, plasma norepinephrine and epinephrine, fasting blood glucose, glucose tolerance test (blood glucose at 1 and 2 hours after ingestion of 1 g glucose/kg body weight), fasting plasma lipids (total cholesterol, triglycerides, high density lipoprotein [HDL]) use of antihypertensive medication, body mass index (BMI), tobacco and alcohol consumption and physical activity in relation to snoring, in a 70-year-old population.

	Snorers (SD)	Non-snorers (SD)	p*	p**
SBP (mmHg)	142.1 (18.6)	137.7 (18.9)	< 0.01	< 0.05
DBP (mmHg)	82.0 (10.1)	80.1 (10.3)	< 0.05	NS
Pulse rate (beats per minutes)	73.8 (11.4)	72.9 (11.0)	NS	NS
Norepinephrine (ng/ml)	0.36 (0.14)	0.33 (0.13)	< 0.05	< 0.005
Epinephrine (ng/ml)	0.026 (0.023)	0.027 (0.023)	NS	NS
Fasting blood glucose (mmol/dl)	4.9 (1.6)	4.8 (1.5)	NS	NS
Glucose, 1 hour (mmol/dl)	8.0 (2.3)	7.5 (2.1)	< 0.01	< 0.02
Glucose, 2 hours (mmol/dl)	6.3 (2.8)	5.8 (2.1)	< 0.01	0.05
Cholesterol (mmol/dl)	6.6 (1.2)	6.6 (1.3)	NS	NS
Triglyceride (mmol/dl)	1.5 (0.7)	1.4 (0.7)	NS	NS
HDL (mmol/dl)	1.4 (0.4)	1.5 (0.5)	NS	NS
Daily use of antihypertensive medication	5.3%	3.2%	NS	NS
Potential confounders:				
BMI (kg/sqm)	26.1 (4.3)	24.7 (4.2)	< 0.0001	< 0.0001
Tobacco consumption (g/day)	12.6 (13.6)	11.0 (12.3)	NS	NS
Alcohol consumption	8.3 (11.0)	6.1 (9.5)	< 0.01	< 0.01
Physical activity (minutes per week)	53.4 (45.5)	48.3 (43.5)	NS	NS

* t-test or X^2 square test

** P value as results of a multivariate analysis with forced entry of potential confounders and snoring as the dependent variable. Among potential confounders the analysis was performed as a stepwise multiple regression.

DISCUSSION

Elevated plasma norepinephrine and abnormal glucose tolerance in self-reported snorers compared to non-snorers, independent of other potential confounders, have never previously been reported. The association between BMI, alcohol and tobacco consumption, plasma lipids and self-reported snoring (1, 5, 6, 10, 12, 13) and sleep apnea (12, 25) have been reported.

In accordance with previous studies (14-18), snorers had a higher blood pressure than non-snorers. When adjustments were made for relevant confounders associated with blood pressure, i.e., BMI, alcohol and tobacco consumption and physical activity, the association ceased and became non-significant for diastolic blood pressure, whereas systolic blood pressure still showed a (weak) association. Accordingly, this study supports the existence of an independent association between snoring and systolic blood pressure in this 70-year-old population. Blood pressure was lower among males than females, which may be explained by a higher mortality among males below age 70 with an adverse cardiovascular risk profile (20).

The male snoring prevalence was comparable with the results from another study (10) including 54-74 year-old males. The snoring question was comparable to that used in other epidemiologic studies regarding sleep-related issues (10-12). The questionnaire was validated against nocturnal laryngeal sound (10) and respiratory recordings (11). In general the snoring question is sensitive, but not specific (10). Self-assessed snoring, on the other hand, is less sensitive but not specific in order to identify those with sleep apnea in a general population (11). With increasing age fewer sleep with a partner. Self-reported snoring habits will undoubtedly be less precise, since no partner tells them that they actually snore (1, 10, 25). A low specificity tends to

diminish a potential relationship, tending to a type 2 error.

The relation between snoring and plasma norepinephrine is interesting. The mechanism of an association between snoring and catecholamines remains unknown. Patients with obstructive sleep apnea may show hypertension (26), elevated plasma epinephrine and norepinephrine and a suppressed pancreating polypeptide level (8, 9, 23). Treatment (tracheostomy or nasal Continuous Positive Airway Pressure [CPAP]) may reduce the adrenergic activity (8, 9).

Snoring was related to plasma glucose and self-reported snorers showed a higher occurrence of diabetes (17). The mechanism is unknown, although abnormalities have been found in hormonal responses, including cortisol (7, 9), growth hormone (7) and in the adrenergic-cholinergic axis (8, 9, 23) in patients suffering from sleep apnea. Sleep apnea only accounts for a minor proportion of snorers (11), and caution should be taken when applying the results from patients with sleep apnea to epidemiological studies regarding snoring.

We conclude that snoring is independently associated with gender, BMI, alcohol consumption, systolic blood pressure, plasma norepinephrine and an abnormal glucose tolerance test in a 70-year-old population.

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