Chimó, a Smokeless Tobacco Preparation, is Associated with a Lower Frequency of Hypertension in Subjects with Type 2 Diabetes

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Abstract

Background: Tobacco use and hypertension are leading preventable causes of death globally. Tobacco is presented as smoked or smokeless tobacco (ST). ST use has been related to cardiovascular disease, type 2 diabetes (T2D), and cancer. In Venezuela, chimó is the most common ST preparation, and its relationship with hypertension is unknown.

Objective: To evaluate the relationship between chimó use and hypertension in a population with a high prevalence of ST use in Venezuela.

Methods: From 2013-2014, a total of 1,938 consecutive subjects aged 20 years or older were evaluated in a medical center. Anthropometrics and blood pressure (BP) measurements, and responses to a standard questionnaire were obtained.

Results: The participants had a mean age of 49.2 years, 59.5% were female, 38.9% had hypertension, 23.2% reported ST use, and 11.6% reported having T2D. One-third of the subjects with T2D were ST users, and this group showed lower heart rate, systolic BP, body mass index (BMI), and frequency of hypertension when compared with T2D subjects who were not ST users (p < 0.05). In subjects with T2D who were 50 years or older, ST use was associated with a 69% lower frequency of hypertension when compared with subjects without ST use. On logistic regression adjusted by heart rate, age, occurrence of T2D, overweight/obesity, and family history of hypertension, ST use was associated with a 30% lower frequency of hypertension (odds ratio 0.70; 95% confidence interval 0.55 – 0.90).

Conclusion: Chimó, a ST frequently used in the Andes region of Venezuela, is associated with lower BP, heart rate, BMI, and frequency of hypertension in subjects with T2D older than 50 years. This counter-intuitive negative association of chimó with some cardiometabolic risk factors highlights the complex nature of these relationships and the need for further studies. (Int J Cardiovasc Sci. 2017;30(5):373-379)

Keywords: Tobacco Use; Tobacco Products; Hypertension; Coronary Artery Disease; Venezuela.

Introduction

Tobacco use and hypertension are leading causes of disease burden worldwide. Together, they caused globally 15.4 million preventable deaths in 2012,1 and 13.3% of disability-adjusted life years (DALY’s) in 2010.2 Tobacco use is defined as current use of any tobacco product in either smoked or smokeless form.1 Many forms of smokeless tobacco (ST) products exist worldwide, and it has been reported that tobacco use increases the risk of coronary heart disease,4 stroke,5 metabolic syndrome,6 type 2 diabetes (T2D),7 and oropharyngeal cancer.8

The prevalence of ST use ranges from 2% to 40% according to the region of the world.9 A high prevalence of ST use (38%) has been described in the Andes region of Venezuela. The prevalence was higher in men than women (58% versus 18% respectively, p < 0.0001), and increased with age.10 Chimó is the most common ST
preparation in this region, and is composed of tobacco leaf, sodium bicarbonate, brown sugar, ashes from the mamón tree (*Melicocca bijuga*), and vanilla and anisette flavoring. The ingredients vary according to the region in Venezuela. A small amount of chimó is placed between the lip or cheek and the gum and is left there for some time, usually 30 minutes. The mixture of chimó and saliva is spit out.\(^{11}\)

The relationship between ST use and hypertension is not completely understood. In Sweden, the use of ST is not banned as in other European countries, and has an increased rate among men (27.2%).\(^{12}\) In a prospective observational study, Hergens et al.\(^5\) reported a 36% increased risk of hypertension among male Swedish users of snuff (made from ground or pulverized tobacco leaves) compared with non-users. In another cohort study using data from the Swedish Annual Level-of-Living Survey, Johansson et al.\(^{13}\) found no difference in the age-adjusted incidence rates of hypertension between daily snuffers and non-tobacco users. Additionally, subjects with T2D are sensitive to nicotine via neuronal nicotinic acetylcholine receptors (nAChRs),\(^{14, 15}\) which can impair insulin action in the presence but not in the absence of T2D.\(^{16}\)

The prevalence of hypertension in the Andes region of Venezuela is elevated (25.0%)\(^{17}\) and similar to that in the Barquisimeto city (24.7%),\(^{18}\) located in the Western region of the country and identified as having the second highest prevalence of hypertension according to the Cardiovascular Risk Factor Multiple Evaluation in Latin America (CARMELA) study, almost duplicating the overall prevalence in Latin America (16.3%).\(^{18}\) Given the global dimensions of hypertension and tobacco use, along with the elevated prevalence of hypertension and chimó use in the Andes region of Venezuela, a critical goal of this study was to understand the relationships and interactions among hypertension, tobacco use, T2D, and other risk factors.

**Methods**

**Population characteristics**

From 2013 to 2014, a total of 1,938 subjects aged 20 years or older consecutively attended a medical center located in Timotes in the Andes Region of Venezuela. Timotes is a mainly agricultural population in the Andean region of Venezuela, with 18,179 inhabitants, located at an altitude of 2,025 meters and with an average annual temperature of 16 °C. The study participants completed a questionnaire. Information about age, gender, personal history of T2D, family and personal history of hypertension and tobacco use was obtained. The use of chimó was questioned, with potential responses given in Table 1. Anthropometric measurements were also obtained. Weight was measured with the subjects wearing as few clothes as possible and no shoes, using a calibrated scale. Height was measured using a metric tape fixed on the wall. Body mass index (BMI; kg/m\(^2\)) was calculated. Blood pressure (BP) was measured twice with an automated BP device (OMRON® HEM-907XL; Omron Healthcare, Inc., 2007, Illinois, USA)\(^{19}\) placed in the right arm at the heart level, with the individual in the sitting position and after 5 minutes of rest. All subjects signed an informed consent for participation.

| Table 1 – Questionnaire of Smokeless Tobacco Use |
|-----------------------------------------------|
| **Questions**                                  | **Answers**                      |
| Have you ever used smokeless tobacco, such as chimó, chewing tobacco, or snus? | Yes, I currently use |
|                                               | Yes, but not within the past 12 months |
|                                               | No, I never used                  |
|                                               | ________ years                    |
| Number of years of use                        | Daily                            |
| Frequency of use                              | Weekly                           |
|                                               | Less than weekly                 |
Variables definitions

Hypertension was defined as a systolic BP ≥ 140 mmHg, diastolic BP ≥ 90 mmHg, or current use of antihypertensive medications. ST use was defined as daily or weekly consumption of chimó for the past 12 months. T2D was defined based on self-report.

Statistical analysis

All calculations were performed using the SPSS 20 program (IBM Corp., 2011, Armonk, NY, USA). Data for continuous variables are presented as mean ± standard deviation. After evaluation for normality, differences between mean values were assessed by unpaired Student’s t test. Frequencies are presented as prevalence rates and 95% confidence intervals (95%CIs). The chi-square test was applied to compare different frequencies. Logistic regression was performed to estimate risk factors associated with hypertension. Statistical significance was considered at an alpha level of p < 0.05.

Results

Subjects characteristics

The study included 1,938 adults with a mean age of 49.2 years, 59.5% females, 38.9% with hypertension, 23.2% users of ST, and 11.6% with T2D. One-third of the subjects with T2D were ST users (Table 2). The subjects with T2D who were ST users showed lower values of heart rate, systolic BP, and BMI, as well as a lower frequency of hypertension when compared with those who were not ST users. In subjects without T2D, ST use was more frequent in men and older individuals. Also, among those without T2D, the heart rate was lower in ST users than in non-ST users.

Smokeless tobacco and hypertension

The use of ST showed a significant relationship with hypertension in subjects with T2D who were older than 50 years (Table 3). In this group, ST users had a 69% lower frequency of hypertension compared with non-ST users. The association between ST use and lower frequency of hypertension remained significant after the variables were adjusted according to BMI (Figure 1). Logistic regression adjusted by heart rate, age, T2D, overweight/obesity, and family history of hypertension showed that ST use was associated with a 30% lower frequency of hypertension (odds ratio = 0.70, 95%CI 0.55 - 0.90) (Table 4).

Discussion

The use of chimó, a form of ST frequently consumed in the Andes region of Venezuela, is associated with lower BP, heart rate, BMI, and hypertension in subjects with T2D older than 50 years. This is the first report associating chimó and lower rates of hypertension, and the reason for this counter-intuitive association is unknown. This result fuels the controversy surrounding ST use and hypertension and may be due to one or more factors.

India has a high prevalence of ST use. In a cross-sectional study in that country evaluating 443 men older than 15 years of age in a rural setting, the prevalence of exclusive ST use (no smoked tobacco) was 21%. The group that used only ST exhibited higher values of diastolic BP and a higher prevalence of diastolic hypertension compared with non-ST users, or with users of ST plus smoked tobacco. The association between high BP and ST use can be related to nicotine levels and sodium concentrations in the ST composition. This result could be explained as some ST products contain large amounts of sodium, as part of the sodium bicarbonate, an alkaline buffer that is necessary to facilitate nicotine absorption. The sodium load (30 to 40 excess mEq sodium per day) could increase BP. However, in 1,061 professional baseball players, ST use was not related to higher BP compared with non-ST users. In that study, serum nicotine and cotinine (a major metabolite of nicotine) were measured. Participants who used snuff had higher serum levels of both cotinine and nicotine than those who used chewing tobacco. In participants with higher nicotine levels, higher diastolic BP was found. Thus, the sodium content and the nicotine content and absorption can vary in different ST preparations potentially accounting for different BP effects.

Another possible explanation for our result is the occurrence of masked hypertension in tobacco users. This effect has been previously reported in smokers, but not in ST users. Smokers tend to have a high daytime ambulatory BP (when they are more likely to be smoking) in comparison with their office BP (when they are less likely to be smoking). The Second Australian National Blood Pressure Study also found that smoking predicted masked hypertension.
Table 2 – Subject characteristics

|                        | Type 2 diabetes | Without type 2 diabetes |
|------------------------|-----------------|-------------------------|
|                        | Smokeless Tobacco | Smokeless Tobacco |
| Total: n               | 68              | 157                     | 381         | 1332        |
| Male (%)               | 51.5            | 40.1                    | 55.6**      | 35.7        |
| Age (years)            | 61.9 ± 9.6      | 62.6 ± 13.8             | 50.0 ± 17.7** | 46.7 ± 16.9 |
| Heart Rate             | 77.8 ± 11.7*    | 82.2 ± 13.2             | 74.3 ± 13.9* | 78.6 ± 14.3 |
| SBP (mmHg)             | 129.1 ± 22.8*   | 136.6 ± 25.1            | 126.9 ± 20.6 | 126.3 ± 20.6 |
| DBP (mmHg)             | 76.2 ± 12.2     | 78.7 ± 12.8             | 78.2 ± 12.4 | 79.0 ± 12.3 |
| BMI (kg/m²)            | 25.8 ± 4.2**    | 28.5 ± 4.8              | 27.5 ± 4.7  | 27.9 ± 5.1  |
| Family Hypertension (%)| 52.9 (41.04 – 64.76) | 51.0 (43.18 – 58.82) | 50.4 (45.38 – 55.42) | 54.7 (52.03 – 57.37) |
| Overweight/Obesity (%) | 61.8 (50.25 – 73.35) | 74.5 (67.68 – 81.32) | 69.8 (65.19 – 74.41) | 70.2 (67.74 – 72.66) |
| Hypertension (%)       | 50.0 (38.12 – 61.88)* | 69.4 (62.19 – 76.61) | 33.3 (28.57 – 38.03) | 36.3 (33.72 – 38.88) |
| Current Cigarettes (%) | 4.4 (0.47 – 9.27) | 4.5 (1.26 – 7.74)       | 5.5 (3.21 – 7.79) | 7.9 (6.45 – 9.35) |

Continuous variables are expressed as mean ± standard deviation (SD). Frequencies are expressed as percentages (95% confidence interval). *p < 0.05; **p < 0.0001 indicates differences between ST users and non-users using Student’s t test for means and chi-square test for frequencies. SBP: Systolic blood pressure; DBP: Diastolic blood pressure; BMI: Body mass index. Overweight/Obesity: BMI ≥ 25 kg/m².

Table 3 – Relationship between ST use and hypertension in subjects with type 2 diabetes who were older than 50 years*

|                        | Hypertension | Normotension | OR (95% CI) |
|------------------------|--------------|--------------|-------------|
| T2D                    | Smokeless Tobacco |              |             |
| Present                |              |              |             |
| ST users               | 23.2 (15.80 – 30.60) | 49.2 (36.85 – 61.55) | 0.31 (0.16 – 0.59) |
| ST non-users           | 76.8 (69.40 – 84.20) | 50.8 (38.45 – 63.15) |             |
| Absents                |              |              |             |
| ST users               | 21.4 (17.34 – 25.46) | 27.3 (22.46 – 32.14) | 0.72 (0.51 – 1.02) |
| ST non-users           | 78.6 (74.54 – 82.66) | 72.7 (67.86 – 77.54) |             |

*Subjects younger than 50 years showed a non-significant relationship. Data are expressed as percentage (95% confidence interval [95%CI]). OR: Odds ratio; ST: Smokeless Tobacco; T2D: Type 2 diabetes.

The effect of ST use on BP level observed in this report was only significant in T2D subjects. The sensitivity to nicotine in T2D has been evaluated comparing the effects of acute nicotine infusion in patients with and without diabetes. Nicotine infusion did not affect the amount of insulin needed to maintain glucose levels in healthy volunteers, but higher levels of insulin were required in patients with diabetes, indicating that patients with T2D are more susceptible to a negative effect of nicotine on insulin sensitivity.

In smokers, nicotine acutely increases energy expenditure and may reduce appetite. This effect could explain the trend of smokers having lower body weight than nonsmokers, and weight gain generally occurring...
after smoking cessation. In this report, subjects with T2D that used ST had lower BMIs than those not using ST, similar to the findings observed in smokers. Also, this report found a lower heart rate in ST users, which also may be due to exposure to a negative chronotropic activity of some component of chimó.

The present study has some limitations. First, chimó in Venezuela is mostly produced using traditional methods, which generate many different formulations for sale, with no fixed doses, and therefore, dosing cannot be characterized as with cigarettes. Moreover, the majority of the components and their respective doses derived from the tobacco leaf in chimó preparations are unknown. Second, blood concentrations of nicotine or cotinine were not measured. Third, oral examination was not used to evaluate the use of ST. Finally, T2D was only diagnosed by self-report.
Conclusion

This study demonstrates for the first time a negative association of chimó use and hypertension. Many forms of ST have been associated (with contradictory evidence in some cases) with cardiovascular disease, cancer, and metabolic alterations. The biological basis of the findings in this report remains elusive. Even though ST use was not associated with a higher frequency of hypertension in this study, it is stressed that ST use is not a healthy practice in patients with T2D, and more importantly, ST use should not be interpreted as a means to reduce the risk of hypertension. The effects of chimó are complex, overall unhealthy, and, in practice, a public health problem requiring further scientific study.

Author contributions

Conception and design of the research: González-Rivas JP, Santiago RJG. Acquisition of data: González-Rivas JP.

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