ORIGINAL ARTICLE

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

Juan P. González-Rivas,[1] Raul José García Santiago,[1] Jeffrey I. Mechanick,[2] Ramfis Nieto-Martínez[3,4,5]

The Andes Clinic of Cardio-Metabolic Studies,[1] Mérida – Venezuela; Division of Endocrinology, Diabetes and Bone Disease, Icahn School of Medicine at Mount Sinai,[2] New York – EUA; Department of Physiology, School of Medicine, Universidad Centro-Occidental "Lisandro Alvarado" (UCLA) and Cardio-Metabolic Unit 7,[3] Geriatric Research, Education and Clinical Center (GRECC), Miami VA Healthcare System,[4] Miami, FL, USA; South Florida Veterans Affairs Foundation for Research & Education,[5] Miami – USA

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; Hypretension; 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.[3] 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

Mailing Address: Juan P. González – Rivas
The Andes Clinic of Cardio-Metabolic Studies.
Av. Miranda, 3112, Sector Centre, Timotes, Mérida – Venezuela.
E-mail: juanpgonzalezr@hotmail.com; juanpgonzalezr79@gmail.com

DOI: 10.5935/2359-4802.20170066

Manuscript received June 28, 2016; revised manuscript December 28, 2016; accepted April 05, 2017

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
Number of years of use	_____ years
Frequency of use	Daily
	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.[20] 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.[21] 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%.[22] 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.[22] 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.[23] However, in 1,061 professional baseball players, ST use was not related to higher BP compared with non-ST users.[24] 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.[24] 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).[25] The Second Australian National Blood Pressure Study also found that smoking predicted masked hypertension.[26]

Table 2 – Subject characteristics

	Type 2 diabetes		Without type 2 diabetes	
	Smokeless Tobacco		Smokeless Tobacco	
	Users	Non-users	Users	Non-users
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.[16] 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.[16]

In smokers, nicotine acutely increases energy expenditure and may reduce appetite.[27] This effect could explain the trend of smokers having lower body weight than nonsmokers, and weight gain generally occurring

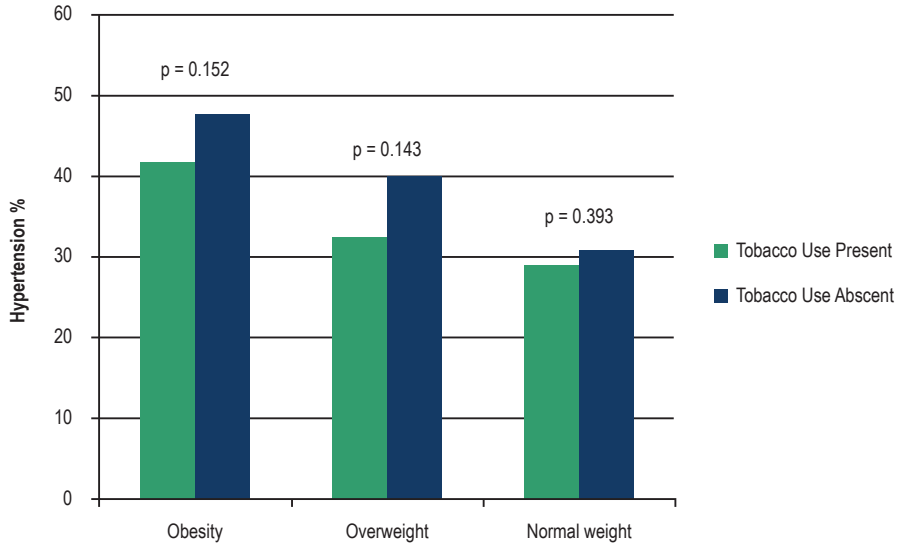

Figure 1 – *Frequency of hypertension according to nutritional status and smokeless tobacco use. Obesity: Body mass index (BMI) ≥ 30 kg/m²; Overweight: BMI 25 to 29.9 kg/m2; Normal weight: BMI < 25 kg/m². p: differences between tobacco users and non-users by chi-square test.*

Table 4 – Risk factors associated with hypertension*

	OR	95% CI
Smokeless tobacco (chimó)	0.70	0.55 – 0.90
Heart rate	1.01	1.01 – 1.01
Age	1.06	1.05 – 1.06
Type 2 diabetes	1.62	1.17 – 2.22
Overweight/Obesity	1.65	1.30 – 2.09
Family hypertension	2.19	1.75 – 2.70

* Multiple logistic regression.

OR: Odds ratio; 95%CI: Confidence Interval. Overweight/Obesity: BMI ≥ 25 kg/m².

after smoking cessation.[28] 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. Analysis and interpretation of the data: González-Rivas JP, Santiago RJG, Mechanick JI, Nieto-Martínez R. Statistical analysis: González-Rivas JP. Writing of the manuscript: González-Rivas JP. Critical revision of the manuscript for intellectual content: Santiago RJG, Mechanick JI, Nieto-Martínez R. Supervision / as the major investigador: Mechanick JI, Nieto-Martínez R.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any thesis or dissertation work.

References

1. World Health Organization. (WHO). Global status report on noncommunicable diseases 2014: a 30% relative reduction in prevalence of current tobacco use. Geneva; 2014. p. 53-66.
2. Lim SS, Vos T, Flaxman AD, Danaei G, Shibuya K, Adair-Rohani H, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012;380(9859):2224-60. doi: 10.1016/S0140-6736(12)61766-8
3. World Health Organization. (WHO). Noncommunicable diseases and mental health. NCD global monitoring framework: indicator definitions and specifications. Geneva; 2014. [Accessed on 2015 Jul 10]. Available from: http://www.who.int/nmh/global_monitoring_framework/en/
4. Teo KK, Ounpuu S, Hawken S, Pandey MR, Valentin V, Hunt D, et al; INTERHEART Study Investigators. Tobacco use and risk of myocardial infarction in 52 countries in the INTERHEART study: a case-control study. Lancet. 2006;368(9536):647-58. doi: 10.1016/S0140-6736(06)69249-0.
5. Hergens MP, Lambe M, Pershagen G, Ye W. Risk of hypertension amongst Swedish male snuff users: a prospective study. J Intern Med. 2008;264(2):187-94. doi: 10.1111/j.1365-2796.2008.01939.x.
6. Norberg M, Stenlund H, Lindahl B, Boman K, Weinehall L. Contribution of Swedish moist snuff to the metabolic syndrome: a wolf in sheep's clothing? Scand J Public Health. 2006;34(6):576-83. doi: 10.1080/14034940600665143.
7. Persson PG, Carlsson S, Svanstrom L, Ostenson CG, Efendic S, Grill V. Cigarette smoking, oral moist snuff use and glucose intolerance. J Intern Med. 2000;248(2):103-10.
8. Lee P, Hamling J. Systematic review of the relation between smokeless tobacco and cancer in Europe and North America. BMC Med. 2009;7(1):36. doi: 10.1186/1741-7015-7-36.
9. Piano MR, Benowitz NL, FitzGerald GA, Corbridge S, Heath J, Hahn E, et al; American Heart Association Council on Cardiovascular Nursing. Impact of smokeless tobacco products on cardiovascular disease: implications for policy, prevention, and treatment: a policy statement from the American Heart Association. Circulation. 2010;122(15):1520-44. doi: 10.1161/CIR.0b013e3181f432c3.
10. González-Rivas J, García Santiago R, Araujo Linares N, Echenique Zureche P. Prevalencia de consumo de tabaco no inhalado (chimó) en el municipio Miranda del Estado Mérida, Venezuela. Rev Ven Endocrinol Metab. 2011;9(3):99-105.
11. Smokeless Tobacco Fact Sheets. In: 3rd International Conference on Smokeless Tobacco. Stockholm (Sweden). September 22 - 25, 2002. Stockholm: Centre of Public Health Centre for Tobacco Prevention; 2002.
12. Furberg H, Lichtenstein P, Pedersen NL, Bulik C, Sullivan PF. Cigarettes and oral snuff use in Sweden: prevalence and transitions. Addiction. 2006;101(10):1509-15. doi: 10.1111/j.1360-0443.2006.01550.x.
13. Johansson SE, Sundquist K, Qvist J, Sundquist J. Smokeless tobacco and coronary heart disease: a 12-year follow-up study. Eur J Cardiovasc Prev Rehabil. 2005;12(4):387-92. Erratum in: Eur J Cardiovasc Prev Rehabil. 2007 Oct;14(5):722.
14. Yoshikawa H, Hellstrom-Lindahl E, Grill V. Evidence for functional nicotinic receptors on pancreatic beta cells. Metabolism. 2005;54(2):247-54. doi: 10.1016/j.metabol.2004.08.020.
15. Ejiri K, Taniguchi H, Baba S. Participation of nicotinic receptor in hormone release from isolated rat islets of Langerhans. Diabetes Res Clin Pract. 1989;6(1):53-9.
16. Axelsson T, Jansson PA, Smith U, Eliasson B. Nicotine infusion acutely impairs insulin sensitivity in type 2 diabetic patients but not in healthy subjects. J Intern Med. 2001;249(6):539-44.
17. Nieto-Martínez R, González-Rivas J, García RJ, Ugel E, Osuna D, Salazar L. Prevalencia de hipertensión arterial y dislipidemias en adultos del páramo del Estado Mérida y su relación con obesidad. Results from VEMSOLS study. Avances Cardiol. 2011;31(3):193-200.

18. Hernandez-Hernandez R, Silva H, Velasco M, Pellegrini F, Macchia A, Escobedo J, et al. Hypertension in seven Latin American cities: the Cardiovascular Risk Factor Multiple Evaluation in Latin America (CARMELA) study. J Hypertens. 2010;28(1):24-34. doi: 10.1097/HJH.0b013e328332c353.

19. El Assaad MA, Topouchian JA, Darne BM, Asmar RG. Validation of the Omron HEM-907 device for blood pressure measurement. Blood Press Monit. 2002;7(4):237-41.

20. Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Bohm M, et al. 2013 ESH/ESC Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). J Hypertens. 2013;31(7):1281-357. doi: 10.1097/01.hjh.0000431740.32696.cc

21. Rani M, Bonu S, Jha P, Nguyen SN, Jamjoum L. Tobacco use in India: prevalence and predictors of smoking and chewing in a national cross sectional household survey. Tob Control. 2003;12(4):e4.

22. Pandey A, Patni N, Sarangi S, Singh M, Sharma K, Vellimana AK, et al. Association of exclusive smokeless tobacco consumption with hypertension in an adult male rural population of India. Tob Induc Dis. 2009;5:15. doi: 10.1186/1617-9625-5-15.

23. Benowitz NL. Sodium intake from smokeless tobacco. N Engl J Med. 1988;319(13):873-4. doi: 10.1056/NEJM198809293191318.

24. Siegel D, Benowitz N, Ernster VL, Grady DG, Hauck WW. Smokeless tobacco, cardiovascular risk factors, and nicotine and cotinine levels in professional baseball players. Am J Public Health. 1992;82(3):417-21.

25. Mann SJ, James GD, Wang RS, Pickering TG. Elevation of ambulatory systolic blood pressure in hypertensive smokers. A case-control study. JAMA. 1991;265(17):2226-8.

26. Wing LM, Brown MA, Beilin LJ, Ryan P, Reid CM; ANBP2 Management Committee and Investigators. Second Autralian National Blood Pressure Study. Reverse white-coat hypertension' in older hypertensives. J Hypertens. 2002;20(4):639-44.

27. Hofstetter A, Schutz Y, Jequier E, Wahren J. Increased 24-hour energy expenditure in cigarette smokers. N Engl J Med. 1986;314(2):79-82. doi: 10.1056/NEJM198601093140204.

28. Chiolero A, Faeh D, Paccaud F, Cornuz J. Consequences of smoking for body weight, body fat distribution, and insulin resistance. Am J Clin Nutr. 2008;87(4):801-9.