ARTÍCULO ORIGINAL

Ausencia de Asociación Entre la Posición de la Lengua Tipo IV de Friedman y Apnea Obstructiva de Sueño en Adultos Mayores con Ancestro Amerindio.

Lack Of Association Between The Friedman's Tongue Position Type IV And Obstructive Sleep Apnea In Older Adults Of Amerindian Ancestry.

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Abstract

Background: The burden of obstructive sleep apnea (OSA) in rural settings is unknown. In these regions, devices needed for OSA diagnosis are not available, and mass screening with field instruments may be complicated due to cross-cultural factors and illiteracy. The association between the Friedman's tongue position (FTP) and OSA has been assessed in people from different ethnic groups but not in Amerindians. **Objective:** We aimed to assess whether a FTP type IV is associated with OSA severity and with the apnea-hypopnea index (AHI) in community-dwelling older adults of Amerindian ancestry living in rural Ecuador. **Methods:** A total of 201 Atahualpa residents aged ≥60 years, who underwent tongue position assessment, brain MRI, and polysomnography were included. After adjusting for relevant confounders, ordinal logistic regression models were fitted to assess the association between the presence of a FTP type IV and OSA categories (none, mild, and moderate-to-severe), and generalized linear models with a Gaussian link were fitted to assess the association between the presence of a FTP type IV and the continuous AHI. **Results:** A FTP type IV was identified in 153 (76%) individuals, the mean AHI per hour was 11.9 ± 12.4, and 49 (24%) individuals had moderate-to-severe OSA, 88 (44%) had mild OSA, and the remaining 64 (32%) had no OSA. Fully-adjusted generalized linear models showed no independent association between the investigated exposure and the AHI (β: 0.09; 95% C.I.: -1.56 – 1.76; p=0.909). Likewise, ordinal logistic regression models showed no independent association between the investigated exposure and categories of OSA (β: 0.42; 95% C.I.: -0.47 – 1.31; p=0.357). **Conclusion:** A FTP type IV is not associated with the AHI or the severity of OSA in this population of Amerindians. This lack of association could be related to phenotypic characteristics of people from this ethnic group (mostly their elliptic hard palate).

Keywords: Obstructive sleep apnea; Apnea-hypopnea index; Friedman's tongue position; Amerindians.

Resumen

Antecedentes: Se desconoce la prevalencia de la apnea obstructiva del sueño (AOS) en entornos rurales. En esas regiones, los equipos necesarios para el diagnóstico de AOS no están disponibles, y la detección de AOS con instrumentos de campo puede ser complicada debido a factores interculturales y analfabetismo. La asociación entre la posición de la lengua de Friedman (FTP) y AOS se ha evaluado en personas de diferentes grupos étnicos, pero no en Amerindios. **Objetivo:** Evaluar si al tipo IV de FTP está asociado con la severidad de la AOS y con el índice de apnea-hipopnea (IAH) en adultos mayores que viven en una comunidad de ascendencia Amerindia en zonas rurales de Ecuador. **Métodos:** Se incluyeron 201 residentes de Atahualpa de edad ≥60 años, que fueron sometidos a evaluación de la posición de la lengua, resonancia magnética cerebral y polisomnografía. Después de ajustar por factores de confusión relevantes, modelos de regresión logística ordinal evaluaron la probable asociación entre la presencia de un FTP tipo IV y las categorías AOS (ninguna, leve y moderada a grave), y se ajustaron modelos lineales generalizados con un enlace gaussiano para evaluar la asociación entre la presencia de un FTP tipo IV y el IAH continuo. **Resultados:** Se identificó un tipo IV de FTP en 153 (76%) individuos, el IAH promedio por hora fue de 11.9 ± 12.4 y 49 (24%) individuos tenían AOS de moderada a grave, 88 (44%) tenían AOS leve. y los 64 restantes (32%) no tenían AOS. Los modelos lineales generalizados, ajustados por confusores, no mostraron una asociación independiente entre la exposición investigada y el IAH (β: 0.09; 95% C.I.: -1.56 - 1.76; p = 0.909). Del mismo modo, los modelos de regresión logística ordinal no mostraron una asociación independiente entre la exposición investigada y las categorías de AOS (β: 0,42; 95% C.I.: -0,47 - 1.31; p = 0,357). **Conclusión:** El tipo IV de FTP no está asociado con el IAH o la gravedad de la AOS en esta población de Amerindios. Esta falta de asociación podría estar relacionada con las características fenotípicas de las personas de este grupo étnico (principalmente su paladar óseo de tipo elíptico).

Palabras clave: Apnea obstructiva del sueño, Índice apnea-hipopnea; posición de la lengua de acuerdo con Friedman.

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Introduction

The burden of obstructive sleep apnea (OSA) in remote rural settings is unknown. In these regions, sophisticated devices needed for OSA diagnosis are not often available, and mass screening with field instruments, such as the Epworth Sleepiness Scale or the Berlin questionnaire, may be complicated due to cross-cultural factors and illiteracy.[1-3]

Finding of a simple and reliable screening tool to facilitate detection of persons at risk of OSA in rural populations is warranted. Several studies have evaluated the potential association between some facial characteristics – particularly the so-called Friedman's tongue position (FTP) – and OSA.[4-6] However, those studies have been conducted in developed countries and more information is required to assess those relationships in different ethnic groups with varied phenotypic characteristics. In this study, we aimed to assess whether the FTP is associated with OSA in community-dwelling older adults of Amerindian ancestry living in rural Ecuador.

Methods

Study population: Atahualpa is located in Coastal Ecuador. The population of this rural village is homogeneous regarding race/ethnicity (Amerindians), living conditions, socio-economic status, and dietary habits; most men belong to the blue collar class and most women are homemakers.[7] The Amerindian ethnicity of Atahualpa residents is supported by their phenotypic characteristics, including an olive-moderate brown skin (Type IV in the Fitzpatrick scale), dark brown eyes and hair, short stature (mean height of the adult population is 149 ± 10 cm), and a predominantly elliptic hard palate.[8] The Atahualpa Project is an ongoing population-based cohort study designed to identify and eventually reduce the increasing burden of cerebrovascular and other non-communicable neurological diseases in the region. Methodology of the sleep substudy of the Atahualpa Project has been detailed elsewhere.[9]

Study design: This study focus on the identification of potential associations between the presence of a Friedman's palate type IV and the apnea-hypopnea index (AHI) and OSA severity (as dependent variables) in community-dwelling Atahualpa residents aged ≥60 years who underwent a single-night diagnostic polysomnography (PSG). Demographics, cardiovascular risk factors, neuroimaging signatures of cerebral small vessel disease (cSVD) and PSG-derived information, were used as confounding variables. The study and the informed consent form that all individuals must sign before enrollment were approved by the Institutional Review Board of Hospital-Clínica Kennedy, Guayaquil (FWA 00006867).

Friedman's tongue position assessment: Participants were asked to open the mouth widely several times, were requested to breathe normally, and to leave the tongue in its natural position (inside the mouth). The FTP was categorized according to previous descriptions.[10] FTP type I allowed the examiner to visualize the entire uvula and tonsils or pillars. FTP type IIa allowed visualization of the uvula but the tonsils are only partially seen. FTP type IIb allowed visualization of the complete soft palate down to the base of the uvula, but the uvula and the tonsils are not seen. FTP type III allowed visualization of some of the soft palate but the distal soft palate is eclipsed. FTP type IV allowed visualization of the hard palate only (Figure 1).

Figure 1. Photographs of two study participants with a Friedman's tongue position type IV. Note that with the mouth widely open and the tongue inside the mouth, only the hard palate is visualized.

Polysomnography: Diagnostic single-night PSGs were performed at the sleep unit of the Atahualpa Project Community Center. Exams were performed with the use of an Embletta® X100™ Comprehensive Portable PSG System (Embla Systems, Inc; Thornton, CO, USA). A board-certified sleep medicine neurologist, blinded to other information, reviewed raw data and interpreted all exams according to the American Academy of Sleep Medicine scoring guidelines.[11] Interest focused on the assessment of the AHI, which calculates the number of apnea/hypopnea events divided by the number of sleep hours (defined as mild OSA if ≥5/h, and to moderate-to-severe OSA if ≥15/h), the total sleep time, the number of desaturation events per hour, and the mean O2 saturation.

Neuroimaging protocol: MRIs were performed with a Philips Intera 1.5T (Philips Medical Systems, Eindhoven, the Netherlands). Interest focused on the identification and rating of neuroimaging signatures of cSVD.[12] For calculating the total cSVD score, each neuroimaging signature was given 1 point if present, for a maximum score of 4. Points were assigned to white matter hyperintensities of presumed vascular origin if they were graded as moderate-to-severe according to the modified Fazekas scale, to cerebral microbleeds and lacunar infarcts – respectively – if there was at least one lesion located deep in the brain (including the subcortical white matter, basal ganglia, thalamus or brainstem) and to enlarged basal ganglia perivascular spaces if there were >10 of these lesions in a single slice in one side of the brain.[13]

Table 1. Characteristics of Atahualpa residents aged ≥60 years across categories of obstructive sleep apnea (univariate analysis).

Variable	Total series (n=201)	Categories of obstructive sleep apnea (OSA) No OSA (n=64)	Mild OSA (n=88)	Moderate-to-Severe OSA (n=49)	*p* value
Age, years (mean ± SD)	71.2 ± 7.5	70.9 ± 7.9	71.2 ± 7.1	71.4 ± 7.6	0.937
Women, n (%)	129 (64)	47 (73)	56 (64)	26 (53)	0.081
Systolic pressure, mmHg (mean ± SD)	142 ± 25	141 ± 27	142 ± 24	143 ± 24	0.914
Diastolic pressure, mmHg (mean ± SD)	75 ± 12	73 ± 12	76 ± 12	77 ± 12	0.166
Fasting glucose, mg/dL (mean ± SD)	135 ± 76	136 ± 82	134 ± 73	136 ± 75	0.983
Total cholesterol blood levels, mg/dL (mean ± SD)	207 ± 35	207 ± 33	208 ± 38	206 ± 31	0.948
Small vessel disease score, points (mean ± SD)	0.68 ± 0.96	0.53 ± 0.85	0.64 ± 0.97	0.96 ± 1	0.049*
Total sleep time, minutes (mean ± SD)	402 ± 59	389 ± 65	396 ± 73	386 ± 63	0.675
Percentage of O2 saturation (mean ± SD)	94.9 ± 4.4	96.3 ± 1.1	95.1 ± 1.3	92.8 ± 8.3	<0.001*
Desaturation events per hour (mean ± SD)	11 ± 12.3	2.4 ± 2	8 ± 5.6	27.7 ± 13	<0.001*
Friedman's palate position type IV, n (%)	153 (76%)	47 (73)	66 (75)	40 (82)	0.568

* Statistically significant result

Clinical covariables investigated: Demographics and cardiovascular risk factors (blood pressure, fasting glucose and total cholesterol blood levels) were selected as clinical confounding variables, and were assessed through interviews and procedures previously described in the Atahualpa Project.[14]

Statistical analyses: Data analyses were carried out by using STATA version 15 (College Station, TX, USA). In univariate analyses, continuous variables were compared by linear models and categorical variables by x2 or Fisher exact test as appropriate. A generalized linear model with a Gaussian link was fitted to assess the independent association between the presence of a Friedman's palate type IV and the AHI (as a continuous dependent variable), after adjusting for demographics, cardiovascular risk factors, neuroimaging signatures of cSVD and other PSG-derived information. Likewise, an ordinal logistic regression model was fitted to assess the independent association between the exposure and the presence and severity of OSA, after adjusting for the aforementioned covariables. Thereafter, the same models were fitted without using PSG-derived information as covariables to assess the role of these confounders (the total sleep time, the number of desaturation events per hour, and the mean O2 saturation) on the association between the exposure and the outcome.

Results

Of 437 community-dwelling individuals aged ≥60 years identified during door-to-door surveys, 201 had assessment of the FTP, cardiovascular risk factors, MRI and PSG. The mean age of the 201 included individuals was 71.2 ± 7.5 years (median age: 70 years, age range: 60 to 95 years) and 129 (64%) were women. Mean (±SD) values were 142 ± 25 mmHg for systolic and 75 ± 12 mmHg for diastolic blood pressure, 135 ± 76 mg/dL for fasting glucose and 207 ± 35 mg/dL for total cholesterol blood levels. The total cSVD score was 0 points in 117 individuals (58%), 1 point in 45 (22%), 2 points in 28 (14%), and 3-4 points in 11 (6%). A Friedman's palate position type IV was identified in 153 (76%) individuals. Mean (±SD) values of PSG-derived parameters included: total sleep time 401.8 ± 59.3 minutes, desaturation events per hour 11 ± 12.3, mean O2 saturation 94.9 ± 4.4%, and the AHI per hour 11.9 ± 12.4 (median AHI: 7.2 episodes per hour). A total of 49 (24%) individuals had moderate-to-severe OSA, 88 (44%) had mild OSA, and the remaining 64 (32%) had no OSA.

In univariate analysis (Table 1), demographics and cardiovascular risk factors did not differ across participants with none, mild, and moderate-to-severe OSA. However, the total cSVD score was higher among individuals with moderate-to-severe OSA (p=0.049). Of PSG-derived information, the total sleep time was similar across groups, but the percentage of O2 saturation was lower among individuals with moderate-to-severe OSA (p<0.001), and – more importantly – the number of desaturation events per hour was significantly higher among individuals with moderate-to-severe OSA (p<0.001). Also in univariate analysis, there were no associations between the presence of a FTP type IV and any of the categories of OSA.

Table 2 depicts the results of multivariate models. Results of generalized linear models with a Gaussian link showed no significant association between the investigated exposure and the AHI (dependent variable), after adjusting for all confounders; in these models, total cholesterol blood levels, the percentage of O2 saturation and the number of desaturation events per hour remained independently significant. Likewise, ordinal logistic regression models showed no significant association between the investigated exposure and categories of OSA (dependent variable), after adjusting for all confounders; in these models, sex (being women), and the number of desaturation events per hour remained independently sig-

Table 2. Multivariate models showing no significant association between the Friedman's tongue position type IV and the apnea-hypopnea index (generalized linear models) or obstructive sleep apnea categories (ordinal logistic regression models) as dependent variables, after adjusting for relevant confounders.

Independent variables (exposures)	β coefficient (95% Confidence Interval)	p value	Covariables remaining significant (p value)
Generalized linear models with a Gaussian link, after adjusting for demographics, cardiovascular risk factors, the total cerebral small vessel disease score, and polysomnographic-derived information.	0.09 (-1.56 – 1.76)	0.909	Total cholesterol (0.006); O2 saturation (0.018); Desaturation events/hour (<0.001).
Ordinal logistic regression models, after adjusting for demographics, cardiovascular risk factors, the total cerebral small vessel disease score, and polysomnographic-derived information.	0.42 (-0,47 – 1.31)	0.357	Sex (0.007); Desaturation events/hour (<0.001).
Generalized linear models with a Gaussian link, after adjusting for demographics, cardiovascular risk factors, and the total cerebral small vessel disease score.	1.45 (-2.55 – 5.45)	0.474	Total cerebral small vessel disease score (0.017)
Ordinal logistic regression models, after adjusting for demographics, cardiovascular risk factors, and the total cerebral small vessel disease score.	0.29 (-0.32 – 0.90)	0.352	Total cerebral small vessel disease score (0.022)

nificant. On the assumption that PSG-derived information (mainly the percentage of O2 saturation and the number of desaturation events per hour) might modify the significance between the exposure and the outcomes, similar models were fitted without including PSG-derived information. However, these models did not show any significant association between the presence of a FTP type IV and the dependent variables (the continuous AHI or OSA categories), after adjusting for demographics, cardiovascular risk factors and the total cSVD score; the total cSVD score was the single covariate remaining independently significant in these models.

Discussion

This study shows lack of association between the presence of a FTP type IV and the continuous AHI and OSA categories. These results are the opposite to that reported from other ethnic groups, where the FTP has found to be a reliable predictor of the presence and severity of OSA. For example, in a recent meta-analysis of 10 studies including 2,513 patients, the correlation of OSA severity with FTP was 0.388 (95% C.I.: 0.049 – 0.646; p=0.026).[15] Most of these studies were conducted in White people, although some were in Asian individuals, and there was one study conducted in Brazil (Sao Paolo), but those individuals were not of Amerindian ancestry.[16]

The high prevalence of a FTP type IV in Ecuadorian Natives/Mestizos may be genetically determined since Amerindians have a predominantly elliptic hard palate.[17] Such high prevalence might have masked any marginal difference with OSA severity or the AHI in this relatively small population. Indeed, the small sample size, together with the cross-sectional design precluding the assessment of causation, are the main limitations of the present study.

In contrast, the unbiased inclusion of participants from the general population as well as the methods used for assess the association between FTP Type IV and the AHI and OSA severity are major strength of the present study. MRIs were performed in all participants, which allowed adjustment for a condition (cSVD) that modifies OSA presence and severity. The racial homogeneity of the population is – at the same time – a limitation and a strength. Our results may not be generalizable to other ethnic groups, but are highly reliable for an ethnic group where the value of the FTP type IV for predicting the presence and severity of OSA has not been investigated. Further studies, preferable following a longitudinal design and including larger number of participants are needed to settle the actual role of the FTP type IV in the prediction of individuals with OSA.

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