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Assessment of salivary cotinine concentration among general non-smokers population: Before and after Spanish smoking legislations

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ABSTRACT

Background: In Spain, two smoke-free laws have been passed (Law 28/2005 and Law 42/2010).This study evaluates the association between Spanish smoking legislations and the second-hand smoke (SHS) exposure in an adult non-smoking population cohort in Barcelona (Spain).

Methods: This is a longitudinal study, before and after the implementation of two national smoking bans, in a representative sample of adults (≥16 years old) from Barcelona (Spain) surveyed in 2004–2005 and followed up in 2013–2014 (n = 736). We only analyzed non-smokers (n = 397). We obtained 9 ml of saliva sample for analysis of cotinine, a biomarker of recent tobacco exposure. We calculated geometric means of salivary cotinine concentration and their geometric standard deviation. We used linear mixed effect models, with individuals as random effects, to model the percentage change in salivary cotinine concentration and their 95% confidence intervals.

Results: The percentage of participants with saliva samples with measurable concentrations of cotinine fell from 92.4% to 64.2% after both Spanish smoking legislations. The geometric mean of salivary cotinine concentration significantly decreased 88% (from 0.98 ng/mL to 0.12 ng/mL, $p < 0.001$) after the implementation of the two Spanish smoke-free legislations. The decrease of the GM salivary cotinine concentration was statistically significant independently of the sociodemographic variables.

Conclusion: There was a large reduction in the salivary cotinine concentration among adult non-smokers and higher cotinine concentrations among those declaring exposure to SHS at home after both legislations. Moreover, after both Spanish smoke-free laws salivary cotinine concentration was homogenized according to sociodemographic variables.

1. Introduction

The effects of secondhand tobacco smoke (SHS) on the health of non-smokers are well-known. SHS exposure has been associated with many adverse health effects [1] and it is classified as a Group I carcinogen in humans [2] by the International Agency for Research on Cancer (IARC). In this sense, the Institute for Health Metrics estimated that about 18% of worldwide population smoked in 2012 causing 11.5% of the global deaths in 2015 attributable to active smoking and 1.6% to passive smoking [3]. In Spain, the latest data reported showed that 23.6% of Spanish population were tobacco users (2012) [4], causing 60,456 deaths attributable to active smoking [4].

Consequently, several countries have implemented tobacco control legislations, as suggested by the World Health Organization Framework

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Convention on Tobacco Control (WHO FCTC) [5]. Regarding Spain, two smoke-free laws have been passed after the approval of the WHO FCTC. On the 1st of January 2006, it came into effect a smoke-free legislation (Law 28/2005). This law was a great step forward for public health in Spain, but it was incomplete in terms of protection to SHS exposure because it allowed smoking in hospitality sectors depending on the size of venues [6]. Because of this exception this Spanish smoking law was known as the "Spanish model" [7]. The scientific evaluation of this law showed the need to promote a total ban [8–10] and motivated the modification of the law accordingly. Hence, a new law (Law 42/2010) came into effect on the 2nd of January 2011, applying the smoke-free regulation to all hospitality venues [11] without exception, and extending the prohibition to some outdoor areas, including hospital premises, educational campuses, and playgrounds.

In order to asses SHS exposure, it is desirable to use biomarkers as they allow to objectively quantifying SHS exposure. In this regard, cotinine, the main nicotine metabolite, has been widely used as a biomarker of tobacco exposure [12]. Cotinine concentration in biological fluids (blood, urine or oral fluid, widely referred to as saliva) [13] indicate tobacco exposure over the previous 1–2 days [14].

Currently, there are scarce studies that evaluate the impact of both Spanish smoking legislations using a general population cohort which increases the internal validity of the results [15]. Moreover, few studies assessed the legislations impact among general population using a specific biomarker of SHS exposure such as cotinine concentration, and only one in Spain using a repeated cross-sectional study [16]. In a previous Spanish cohort of hospitality workers, salivary cotinine concentration decreased significantly (by 56.6%) among hospitality workers at venues where smoking was totally banned after the Spanish partial ban (law 28/2005) took effect [11]. Therefore, the objective of this study is to evaluate the association between both Spanish smoking legislations and the SHS exposure in an adult non-smoking population cohort in Barcelona (Spain) using salivary cotinine concentrations and information on self-reported exposure.

2. Methods

This is a longitudinal study from a representative sample of the adult population (≥16 years) of the city of Barcelona (Catalonia, Spain). The baseline study was carried out during the years 2004–2005 [17,18] (n = 1245) and follow-up took place in 2013-1014, after both Spanish smoking legislations (n = 736).

From the baseline sample, we excluded 235 subjects, 150 after checking their data in the Insured Central Registry of Catalonia (101 died and 49 migrated out of the province of Barcelona) and another 85 without consent to be followed up or being minor (< 18 years old) in 2004–2005 whose parents did not provide informed consent to be re-contacted. Follow-up was conducted between May 2013 and February 2014. In total, 72.9% of the eligible sample agreed to participate, 18.5% refused to participate, 7.2% had moved elsewhere and 1.3% had died. The final sample included 736 individuals (Fig. 1).

Saliva samples were frozen and sent to the 'Hospital del Mar' Medical Research Institute (IMIM) in Barcelona. Salivary samples from baseline survey (2004–2005) were analyzed with gas chromatography followed by mass spectrometry detection (GC/MS). The limit of quantification was 1 ng/mL and the limit of detection was 0.3 ng/mL. Salivary samples from the follow-up survey (2013-14) were analyzed with liquid chromatography coupled with tandem mass spectrometry (LC/MS/MS) [19] with multiple reaction monitoring. The limit of quantification was 0.1 ng/mL and the limit of detection was 0.03 ng/mL (quantification error < 15%). Because the latter method was more sensitive and had a lower limit of quantification than the former method, all available saliva samples from the baseline survey (2004–2005) with cotinine concentrations below 1 ng/mL (n = 245) were reanalyzed with the LC/MS/MS method. For cotinine concentrations below the limit of quantification a value of half the level of quantification (0.05 ng/mL) was assigned.

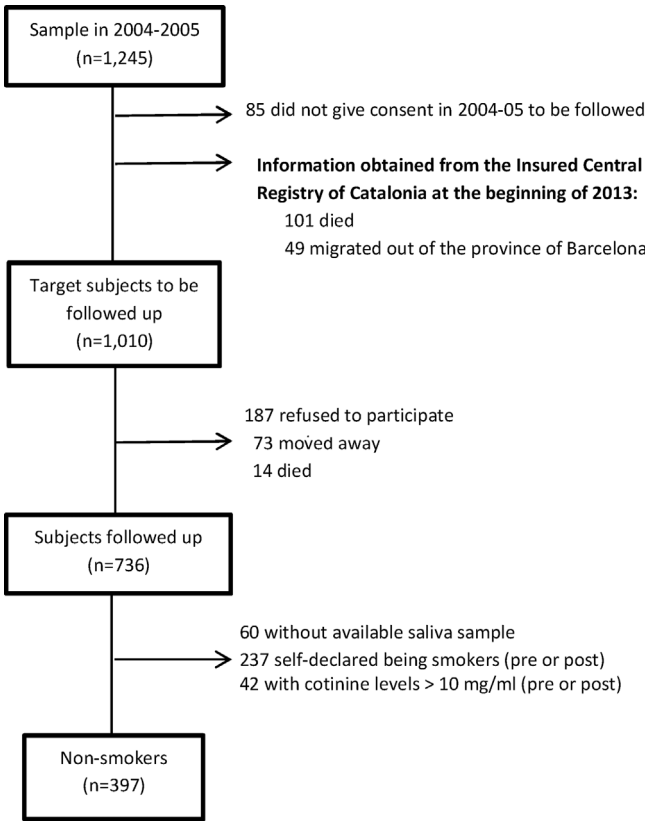

Fig. 1. Flow chart of sample followed-up from Barcelona, Spain, in 2013–2014.

The same definition of smoking status was used in both studies. We considered as non-smoker the person who declares to have never smoked or to have formerly smoked, and has a salivary cotinine concentration compatible with non-smoking (≤10 ng/mL) [20]. The final sample for this study consists of 397 non-smokers before and after the Spanish smoking legislations (Fig. 1).

Given the skewed distribution of cotinine concentration, we calculated geometric means (GM) and their geometric standard deviation (GSD). We used linear mixed effect models with individuals as random effects adjusted for basal sex, age and educational level to model the change percentage in salivary cotinine concentrations (after log 10 transformation) and their 95% confidence intervals. We obtained the *p*-value for the median difference through Wilcoxon test for paired samples and Mann Whitney test for independent samples. Moreover, the results were stratified by sex, age and educational level. The statistical program used was *R*-3.0.2 and Stata v14.

3. Results

The percentage of participation in both stages was 51.9% (736 out 1245). There were no statistically significant differences between the followed-up sample (n = 736) and the participants lost in the second stage (n = 274) according to age, sex, level of education and smoking status. However, there were statistically significant differences according to age, level of education and smoking status between the follow-up sample (n = 736) and the participant lost in both stages of the follow-up (n = 509) (Table 1).

The percentage of participants with saliva samples with measurable concentrations of cotinine fell from 92.4% to 64.2% after both Spanish smoking legislations. We also found a leftward shift in the salivary cotinine distribution after both Spanish smoking legislations (Fig. 2), i.e. it is more frequent to obtain lower values in the salivary cotinine concentration after the legislations.