ORIGINAL RESEARCH

Exhaled carbon monoxide as a marker for evaluating smoking abstinence in a Brazilian population sample

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Abstract

Background: Exhaled carbon monoxide (CO_{Exh}) measurement is used to confirm smoking status in smoking cessation programs, but the cut-off level is still a matter for discussion. The objective of this study was to compare CO_{Exh} levels in smokers and non-smokers to validate the method in a Brazilian population and to estimate the probability of the patient still smoking according to different cut-off points.

Methods: In this cross-sectional study we studied non-atopic Caucasian volunteers with no respiratory infection or steroid therapy in the preceding four weeks. Exclusion criteria were: pregnancy; breast feeding; age <18 and >65 years old; and subjects not signing informed consent. Participants filled out a questionnaire and had their CO_{Exh} levels measured. Bayes' theorem was used to calculate the post-test probabilities.

Results: We included 393 subjects of whom 239 (61%) were smokers. The mean CO_{Exh} was 14.7 +/- 9.4ppm and 4.3 +/- 2.5ppm (p<0.001) in smokers and non-smokers, respectively. Patients with CO_{Exh} below 8ppm had a likelihood ratio below 1 of still smoking. The levels 9ppm and 10ppm provided likelihood ratios of 1.50 and 1.93, respectively. Better discriminant power was obtained at >11ppm, when the likelihood ratio became 63.80 (95%CI 16.1-253.1).

Conclusions: In smoking cessation practice, a likelihood ratio approach may be useful to determine the probability that an individual is still smoking according to various CO_{Exh} cut-off points instead of using a fixed value for all patients.

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Introduction

Smoking is the most widespread addiction, affecting about one third of the world's population.¹ In Brazil, the situation is of some concern,^{2,5} given that each year about 200,000 Brazilians die early because of smoking.^{4,5}

Stopping smoking is only achieved by 6% of smokers who try to quit without medical help.⁶ Professional input in the form of cognitive behaviour therapy and specific pharmacotherapy helps to achieve higher success rates.^{3,7}

However, abstinence during smoking cessation treatment needs to be confirmed by objective measurements since it is known that smokers sometimes provide false information about their smoking status. This happens especially if the individual is under pressure to quit and therefore is biased towards producing a socially desirable response when questioned.⁸ The prevalence of patients who state that they are not smoking when they actually still are varies between 3 and 10%. Lower incidences of unreliable reporting are found in general population surveys while higher proportions are found in patients enrolled in quit-smoking programs.⁹⁻¹¹

To avoid these biases, biochemical markers for abstinence have been introduced in clinical practice. Carbon monoxide level in exhaled air (CO_{Exh}) is the most often used.¹² It is an affordable marker measured by a non-invasive technique which provides immediate and reliable results.¹³ It has been used in various centres in Brazil,¹⁴⁻¹⁶ although its use has not been widely validated in this country.

The aim of this study was to compare the levels of CO_{Exh} in smokers and non-smokers in a sample of the Brazilian population. In addition, given the importance for the clinician of ascertaining whether or not the patient enrolled in a quit-smoking program is still smoking, we decided to estimate likelihood ratios for smoking at different levels of CO_{Exh}.

Material and methods

Two groups of individuals were selected to be included in this cross-sectional study. The first group constituted smokers appearing for their first visit to our outpatient clinic for smoking cessation. The second group constituted individuals recruited among shoppers in a local shopping mall who declared themselves to be non-smokers, stated that they were in good health, and did not consider themselves as passive smokers. Since in both situations there was no pressure involved, we assumed

that subjects had no reasons to hide their smoking status or to give false information. Volunteers were non-atopic Caucasians without any respiratory infections who had not received corticosteroids in the preceding four weeks. An informed consent form was signed before enrolment. Exclusion criteria were: pregnancy; breast feeding; age less than 18 or greater than 65 years; passive smokers; and subjects with a previous diagnosis of COPD or any other pulmonary disease. Participants filled out a standard questionnaire regarding demographic information, smoking habits (number of cigarettes per day, total years of smoking) and Fagerstrom test of nicotine dependence-FTND.

CO_{Exh} was measured by a MicroCO Meter (MicroCO – Micro Medical Ltd, Rochester, Kent, UK), using an electrochemical sensor. Patients were instructed to breathe deeply and to hold their breath for 20 seconds and then to exhale slowly and completely through a mouthpiece. Smokers had their CO_{Exh} measured at no more than two hours since the last smoked cigarette. The coefficient of variation of these measurements was accepted if within 5 and 10%. Subjects also had their weight and height measured.

CO_{Exh} levels and age of volunteers were analysed by Student's t-test for independent samples. Spearman's correlation was utilised to determine the correlation between CO_{Exh} with number of cigarettes smoked and also with time since last cigarette smoked (alpha = 0.05).

Measures of diagnostic performance were based on likelihood ratios (LR). This approach was used to estimate the ratio of the probability of a particular level of CO_{Exh} observed in a smoking patient compared to the same probability in a non-smoker. LRs above 10 and below 0.1 were used as strong evidence to rule in or rule out, respectively, the smoking status of the participants.¹⁷ Area under the ROC curve was obtained with 95%CI, considering several cut off points. Statistical procedures were conducted using SPSS 12.0 (SPSS Inc, Chicago, IL, USA).

Ethical approval for the study was obtained from the institutional ethics board (PUCRS Ethics Committee). All participants provided written informed consent before inclusion in the protocol.

Results

A total of 393 individuals were included, 239 (61%) being smokers. The mean age ($\pm$ SD) was 26.6 ($\pm$ 9.7) and 28.9 ($\pm$ 11.5) years among non-smokers and smokers, respectively ($p > 0.05$). The demographic characteristics were similar between

Table 1 Characteristics of the sample

Characteristic	Smokers n=154	Non-smokers n=239	p value
Demographic			
Female gender (%)	39.2	60.8	0.21
Age, years; mean±SD	28.9±11.5	26.6±9.7	0.07
Schooling (%)			0.19
Elementary	35.1	37.8	
High School	24.5	22.7	
University	40.4	39.5	
Exhaled CO (median;P25-P75)	19 (13-26)	4 (3-5.3)	<0.001
Smoking behavior			
Cigarettes/day (mean±SD)	25.3±4.5	—	
Years smoked (mean±SD)	10.2±3.8	—	
Fagerstrom Dependence (%)			
Mild	26	—	
Moderate	50	—	
Severe	23	—	

Table 2 Estimates of likelihood ratios for different cut-off points of exhaled CO levels in predicting smoking status

Cut-off (ppm)	Smokers (n=239)	Non-smokers (n=154)	Likelihood ratio (LR)	95% CI
≤ 5	11	116	0.06	0.03-0.11
6	5	13	0.25	0.09-0.68
7	6	10	0.39	0.14-1.04
8	6	8	0.48	0.17-1.37
9	7	3	1.50	0.39-5.73
10	6	2	1.93	0.40-9.46
≥11	198	2	63.80	16.1-253.1

ppm = particles per million; area under the receiver operating characteristics curve: 0.96 (95%CI 0.94 to 0.98)

these two groups. The mean CO_{Exh} in the group of smokers (14.7 ± 9.4 ppm) was significantly higher than in non-smokers (4.3 ± 2.5 ppm) ($p < 0.001$) and a significant association was found between the quantity of cigarettes smoked per day and the CO_{Exh} level ($r = 0.7$, $p < 0.001$) – see Table 1.

Table 2 shows a progressive increase in the likelihood of being a smoker as the CO_{Exh} cut-off was progressively set at higher levels. When the value was moved from 10 to 11 ppm, a striking gap in the likelihood ratio was observed. The area under the ROC curve was calculated as 0.96 (95%CI 0.94-0.98).

Discussion

In this study, we have shown that a sample of Brazilian smokers have higher CO_{Exh} levels than non-smokers and that there is a positive assoc-

iation between the number of cigarettes smoked and CO_{Exh} level. This is in accordance with the literature.⁹ We also studied CO_{Exh} testing as a marker of abstinence, calculating the likelihood ratio for each different level. Using this statistical procedure, we were able to calculate the accuracy of each cut-off point and evaluate how many times more (or less) it predicted the real smoking condition.

Thus, instead of establishing a single cut-off level for all patients – which is the norm in most smoking cessation clinics – a more useful approach seems to be to verify the probability of a person smoking based on the level of exhaled CO. When applied to individuals undergoing treatment in any smoking cessation clinic, this measurement predicts the probability of the patient still smoking even when the patient denies it. Sensitivity, specificity and predictive values do

not do this, or are dependent on the prevalence of the event (usually unknown), making it difficult to use these parameters in everyday practice. Likelihood ratios could provide a solution by simplifying the real-life evaluation of the patient – especially in primary care.

There is still controversy in the literature regarding which cut-off point for CO_{Exh} to use.¹⁸ A reliable level of CO concentration in exhaled air which can differentiate smokers from non-smokers has not yet been fully established, probably as a consequence of differences in prevalence of misreporting. Thus, while some authors suggest 6 ppm as the most appropriate value,^{13,16} higher CO_{Exh} levels, usually equal to or above 10 ppm, are the most widely accepted cut-off levels in specialised clinics as the marker for ongoing smoking.^{8,19,20}

In our sample, subjects still smoking a few cigarettes per day, or those who were in the process of quitting but suffering occasional lapses, had a CO_{Exh} level lower than 10 ppm. These latter patients deserve special consideration because they are at high risk of returning to a heavier smoking lifestyle. In this group, CO_{Exh} measurement has a special role, since these are patients whose responses to inquiries regarding smoking behavior are frequently not reliable. Indeed, in such a clinical situation, the interpretation of CO_{Exh} results may be not easy, and a categorical classification of a patient as a smoker or non-smoker may be difficult.

Using the likelihood method, patients with a CO_{Exh} of 7 ppm had a 0.39 (0.14-1.04) 'still smoking' probability, even if they denied smoking. When a value of 9 ppm was used, the probability of actually being a smoker became 1.50 (0.39-5.73). In these groups of individuals, considering that the confidence interval included values below and above 1, it would be important to utilise complementary methods, albeit more expensive and/or more invasive measures, to determine the clinical situation with more certainty. In the group with CO_{Exh} ≥ 11ppm, the probability of an individual still smoking despite stating otherwise was very high, sparing the need for further investigation (LR 63.80, 95%CI 16.1 to 253.1). Likelihood ratios above 10 are considered to provide strong evidence for ruling out a diagnosis – in this case, the diagnosis of being a 'smoker'.¹⁷

The strength of this study is that the included patients had no reason to misreport their smoking condition, since they were under no pressure. The main limitation to our conclusions is that in some subgroups the number of individuals was low. Therefore, the conclusions of this study should be considered as preliminary.

We realise that the median CO_{Exh} of our non-

smokers is higher than expected, but we did not consider this to be of clinical relevance. All shopping malls in Porto Alegre, Brazil, are strictly non-smoking areas. However, the specific shopping mall where the study was conducted is located in an area of intense traffic activity. The impact of such environmental exposure in our participants is unknown. Also, a faulty heating system cannot be excluded. However, if these potential biases were real, they would have influenced the results of both groups, i.e., smokers and non-smokers.

Based on these preliminary findings, it is possible to speculate that it may be more useful to determine the probability of each individual being a smoker instead of using a categorical classification according to a single value of CO_{Exh} for all patients tested. In this way, management of each specific case would be individualised, thereby improving the potential benefits of intervention.

Conflict of interest declaration

There are no conflicts of interest to declare.

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