

The Effect of Water-Pipe and Cigarette Smoking on Exhaled Nitric Oxide

Abstract

Context: Fractional exhaled nitric oxide can be used as a biomarker of some respiratory diseases. **Aims:** This study was conducted to compare exhaled nitric oxide in cigarette and water-pipe smokers with nonsmokers. **Methods:** This cross-sectional study was conducted on 549 adult subjects as a sub-study of Shahedieh cohort in Yazd. Participants were divided into 5 groups according to their smoking habits: non-smokers ($n = 202$), cigarette smokers ($n = 121$), water-pipe smokers ($n = 129$), cigarette ex-smokers ($n = 58$), water-pipe and cigarette smokers ($n = 39$). The smokers were also categorized into heavy and light smokers. Fractional exhaled nitric oxide was compared between the groups. **Statistical Analysis Used:** The data were analyzed by SPSS (ver. 20) using Kolmogorov-Smirnov, Kruskal-Wallis, and Mann-Whitney U tests. **Results:** Fractional exhaled NO was lower in all smokers than nonsmokers, but cigarette smokers showed the least level of NO than other groups. Fractional exhaled NO was not significantly lower in water-pipe smokers than nonsmokers. **Conclusions:** Cigarette smoking significantly affect fractional exhaled NO, but water-pipe smoking did not significantly affect exhaled NO level.

Keywords: Cigarette smoking, nitric oxide, water pipe smoking

Introduction

Nitric oxide (NO), an endogenous gas, is a component of human's breath. It plays an important role in some respiratory processes such as vascular regulation, host defense,^[1] and it may have cytoprotective effects.^[2] The fractional concentration of NO in exhaled breath (FeNO) is now used as a biomarker which may help diagnose some respiratory diseases.^[3-5]

Cigarette smoking can reduce FeNO.^[6] FeNO increase shortly after smoking but long-term exposure to cigarette smoke reduced it. It has been shown as well that this effect was influenced by smoking history,^[7] and it may be reversed after smoking cessation.^[8] In cigarette smokers, NO metabolism is changed due to the oxidation of NO.^[9] So, results of FeNO in different disease states should be interpreted cautiously in smokers.^[10] Some other factors such as BMI or some other occupational or environmental exposures may affect FeNO as well.^[11,12]

Water-pipe (other names: hubble-bubble, hookah, narghile, argghile, qalyan, and sheesha) is a traditional device to smoke tobacco in the Middle East and its use was

common in Iran, in the past. Recently, its use is increased again especially among females and the young with a probable belief that it is harmless.^[13] The prevalence of water-pipe smoking in the adolescents in the Middle East countries is about 6-34%.^[14]

Each session of hookah smoking includes about 50-200 puffs which contains about 10 g tobacco and produces about 25 mg of nicotine,^[15,16] which is equivalent to smoking about 100 cigarettes.^[17] Nowadays, besides pure tobacco, some fruit extracts have been added to tobacco leaves which are smoked by this device.

The studies on the effect of water-pipe on different organs and especially respiratory system mostly have shown a negative effect, though with controversial results.^[18,19] Most studies on the effect of water-pipe smoking on respiratory function have shown a negative effect in comparison to non-smokers,^[15,20] and a systematic review found that water-pipe smoking is probably as harmful as cigarette smoking.^[21] Raad *et al.* in a systematic review concluded that water-pipe negatively affects respiratory system and is probably one of the causes of COPD,^[22] although some studies did not find a significant difference in lung function

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between water-pipe smokers and non-smokers.^[23,24] The effect of water-pipe smoking on pulmonary function tests in comparison to cigarette smoking is controversial.^[25]

We could find few studies on the effects of water-pipe on FeNO. Some studies showed a lower FeNO among water-pipe smokers than non-smokers^[26] and an immediate effect of water-pipe on FENO.^[27,28]

Due to the not conclusive results about the effect of water-pipe smoking on FeNO (in comparison to cigarette smoking and not smoking) and the large differences in various populations in the devices and methods of smoking water-pipe, this study was performed to assess the effect of water-pipe smoking on FeNO in comparison to non-smokers, cigarette smokers, and ex-smokers in an Iranian suburban adult population.

Subjects and Methods

This was a cross-sectional study on 549 adult subjects as a sub-study of Shahedieh cohort ($n = 10194$) in Yazd. Shahedieh cohort is a branch of a national cohort study (PERSIAN cohort) on adult population (age range: 35–70 years) which has begun in Yazd from 2015.^[29] The subjects were randomly selected from Shahedieh cohort participants who did not suffer from a diagnosed respiratory disorder in Yazd and were divided into 5 groups according to their smoking habits: non-smokers ($n = 202$), cigarette smokers ($n = 121$), water-pipe smokers ($n = 129$), cigarette ex-smokers ($n = 58$), water-pipe, and cigarette smokers ($n = 39$). Demographic data were extracted from the cohort database. Smoking history and its related information have been collected by standard questionnaires during the enrollment phase of the cohort study.^[29] All cigarette smokers and almost all water-pipe smokers were males, so females in the non-smoker group were also excluded from the study, so all participants were males.

The subjects with at least 1 pack year cigarette smoking and 2 water-pipe sessions (heads) per week were considered as cigarette and water-pipe smokers, and those who had quit cigarette smoking for at least 1 year were considered as ex-smokers. The cigarette smokers were also categorized into heavy (smoked more than 10 pack-years, $n = 48$) and light smokers ($n = 73$) according to their pack-years of smoking; and water-pipe smokers were also categorized to heavy (smoked more than 395 water-pipes lifelong, $n = 34$) and light ($n = 95$) smokers. This categorization was done according to the median of pack/years of cigarette smoking and number of lifelong water-pipe smoking sessions.

FeNO measurement

FeNO was measured by a portable electrochemistry-based device (NObreath, Bedfont Scientific Ltd., UK). American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines were used to perform tests.^[30] NO concentration

was measured in part per billion (ppb). The test was performed in sitting position and the participant was asked to perform expiration for 10 s with a constant flow (50 ml/s) and pressure (10 CmH₂O). After performing at least two acceptable maneuvers, the test was terminated and the mean of two measurements with less than 4 ppb difference was reported as the final result. Heavy exercise, having large meals, and smoking 1 h before test were considered as the intervening factors and the test was postponed to 1 h later.

The data were analyzed by SPSS (ver. 20) using Kolmogorov-Smirnov, Kruskal-Wallis, and Mann-Whitney U tests. This study was a residency thesis in occupational medicine in Shahid Sadoughi University of Medical Sciences. The protocol of the study was approved by the ethics committee of the university.

Results

Totally 549 participants were assessed regarding their exhaled breath NO concentration. Mean age of the participants was 48.4 ± 8.0 years (range, 38-70). The highest mean age was observed in ex-smokers (52.2 ± 6.8 years) which was significantly higher than other groups, but the difference in age was not significant between other study groups. Body mass index was not significantly different between groups. Table 1 shows descriptive statistics of the study participants.

There was a significant difference between groups regarding FeNO ($P < 0.001$). The lowest FENO was observed in cigarette smokers. Table 2 shows pairwise comparisons between groups regarding FeNO.

FeNO was much lower in heavy cigarette smokers, but the difference was not statistically significant. Table 3 compares FeNO between heavy and light cigarette and water-pipe smokers.

Discussion

Water-pipe smoking is increasing recently in our country with a premise that water-pipe smoking does not harm their health. In this cross-sectional study as a sub-study of Shaedieh cohort, we compared the long-term effect of cigarette and water-pipe smoking on FeNO.

In accordance with many previous studies, this study showed that smoking reduced FeNO, but this decrease in comparison to non-smokers was statistically significant only in the cigarette smokers, but not in water-pipe smokers.

Water-pipe is a device for tobacco smoking, especially in the Middle East. Water-pipe smoking may induce diseases which are attributed to cigarette smoking, such as lung cancer, esophageal cancer, and periodontal diseases.^[31] Some studies have shown a negative effect on pulmonary function tests for water-pipe smoking,^[22] although with different effect sizes comparing cigarette smoking. Most

Table 1: Descriptive statistics of the study participants in different groups according to smoking status

Variable	Smoking status				
	Non-smoker	Cigarette	Water-pipe	Cigarette and water-pipe	Ex-smoker
Number	202	121	129	39	58
Age (yr.)	48.0±8.0	49.9±6.8	47.4±8.4	48.2±8.4	52.1±8.1
Pack-years	NA*	11.95±7.76	NA	9.76±6.61	9.04±13.71
Lifelong water-pipe heads	NA	NA	394.68±1026.81	485.08±816.90	NA
Water-pipe heads per week	NA	NA	2.71±5.24	3.01±5.12	NA
FeNO** (ppb)					
Mean±SD	8.75±8.23	6.36±11.50	7.83±6.05	6.41±7.70	6.84±6.03
Median	5.67	3.33	5.00	4.33	4.66

*NA: Not applicable; **FeNO: Fractional exhaled nitric oxide

Table 2: Pairwise comparisons of FENO between smokers and non-smokers

Smoking status	n	Mean (SD)	P
Cigarette smoker	121	6.36 (11.50)	<0.001
Non-smoker	202	8.32 (9.87)	
Ex-smoker	58	6.84 (6.03)	0.16
Non-smoker	202	8.32 (9.87)	
Water-pipe smoker	129	7.73 (6.49)	0.65
Non-smoker	202	8.32 (9.87)	
Water-pipe and cigarette smoker	39	6.41 (7.71)	0.23
Non-smoker	202	8.32 (9.87)	
Cigarette smoker	121	6.36 (11.50)	0.54
Ex-smoker	58	6.84 (6.03)	
Cigarette smoker	121	6.36 (11.50)	0.002
Water-pipe smoker	129	7.73 (6.49)	
Cigarette smoker	121	6.36 (11.50)	0.46
Water-pipe and cigarette smoker	39	6.41 (7.71)	
Water-pipe smoker	129	7.73 (6.49)	0.09
Water-pipe and cigarette smoker	39	6.41 (7.71)	

Table 3: Comparison of FeNO between heavy and light cigarette and water-pipe smokers

	n	FeNO (PPb)	
		Mean±SD	P
Cigarette			
Heavy	73	4.61±4.78	0.10
Light	48	7.53±14.19	
Water-pipe (lifelong)			
Heavy	30	7.22±6.54	0.59
Light	99	7.88±6.49	
Water-pipe (per year)			
Heavy	32	7.94±6.64	0.12
Light	97	6.21±6.13	

previous studies have assessed the effect of water-pipe on spirometric parameters. In Kiter *et al.* study, the effect of water-pipe on spirometric parameters was not as great as cigarette,^[23] although Boskabadi *et al.* and Baiee *et al.* found that the negative effect of water-pipe smoking on spirometric parameters is almost similar to cigarette

smoking.^[15,20] Few studies have assessed the effect of water-pipe smoking on FeNO.^[26,27]

NO is a free radical which can react with other molecules and is useful in the diagnosis of some respiratory diseases such as asthma and atopy.^[32] Cigarette smoke contains NO and can increase FeNO immediately after smoking, but may reduce its production in the body as a negative feedback mechanism,^[33] by inhibition of NO synthase (NOS)^[34] or by presenting such molecules as superoxide which may react with NO.^[35]

In the current study, cigarette smokers had the lowest FeNO which was significantly lower than non-smokers and water-pipe smokers. Most previous studies have shown a lower FeNO in cigarette smokers than non-smokers.^[7,9]

Quitting cigarette smoking may reverse its effects on FeNO.^[36] In this study, ex-smokers had also a lower FeNO than non-smokers, but this difference was not statistically significant, and their FeNO was higher than current smokers, which shows a trend toward non-smokers.

About the effect of age on FeNO, there are controversial results; in this study, all groups were similar regarding age except for ex-smokers who were significantly older than other groups, so our main results were not influenced by age.

Mean FeNO in smokers and non-smokers of our population was much lower than Meo *et al.* study in Saudi Arabia,^[26] which is probably due to genetic factors, anthropometric dimensions and different devices used to assess FeNO or even different kinds of water-pipe devices or tobaccos. In the present study, FeNO in water-pipe smokers was significantly higher than cigarette smokers, but non-significantly lower than non-smokers, which was in contrast to the results of Meo *et al.* study who found a significantly lower FeNO in water-pipe smokers than non-smokers.^[26] This difference is probably due to different methods of water-pipe smoking, different devices or different tobaccos used in two countries or even different genetic factors.

Hakim *et al.* assessed the effects of water-pipe on FeNO and showed that water-pipe can reduce FeNO immediately

after smoking.^[27] We measured FeNO after at least 1 hour of smoking, so acute effect was not possible to assess in this study.

Considering the amount of smoking (pack-years of cigarettes and numbers of water-pipe sessions), this study failed to show a statistically significant difference between heavy and light smokers, although FeNO was much lower in heavy cigarette smokers than light smokers, but this difference was not statistically significant. Probably a larger sample size may show this effect. Similarly, in the water-pipe smokers, the number of smoked water-pipes was not associated with decreased FeNO.

This study had some limitations: Our population was older than 35 years and all participants were males, so we could not assess the young population and females. We did not have data about the type of tobacco, cigarettes and water-pipe device which may affect the results.

Conclusion

The results of this study showed that cigarette and water-pipe smoking decreased FeNO in middle-aged male population in comparison to non-smokers, but this decrease was statistically significant only in cigarette smokers. Quitting cigarette smoking may reverse the effects of smoking on FeNO.

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Conflicts of interest

There are no conflicts of interest.

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