Smoking and cerebral blood flow: A comparative study between cigarette and shisha

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Background
There is belief that water-pipe smoking is less toxic than cigarettes. However, studies indicated that it exposes patients to more toxins than cigarette smoking.
Purposive
This study aims at assessing tobacco and water pipe-related cerebral blood flow (CBF) and comparing the CBF parameters between them using transcranial Doppler ultrasonography.
Patients and methods
This cross-sectional study was conducted on 40 male smokers and 20 controls. Participants were subjected to full history and detailed clinical and neurological examination. Transcranial color coded duplex was performed.
Results
CBF parameters from either anterior or posterior circulation were significantly higher in both cigarette and shisha smokers. Higher parameters were noticed in shisha smokers. Increased cerebrovascular reactivity was one of our interesting discoveries.
Conclusion
Impaired cerebral circulation in smokers either cigarette or water-pipe, with abnormal cerebrovasculature, was suggested. These were consistent with hypoperfusion in smokers. These results were more evident in water-pipe smokers.

Keywords:
cerebral blood flow, smoking, transcranial color coded duplex

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Introduction

There is growing increase of water-pipe smoking today because of the belief that it is less toxic than cigarettes owing to the absence of direct tobacco exposure to the smoke [1]. However, studies have indicated that toxic exposure from the water pipe is equal to 100 cigarettes [2]. Although water-pipe-related hazard effects have been described, there are insufficient data in the literature about changes in cerebral blood flow (CBF) [2]. In addition, it is particularly important to understand the smoking–CBF relationship at younger age before the burdens of aging and accumulated vascular and cerebrovascular disease become substantial [3]. The aim of the study was to evaluate tobacco and water pipe-related CBF and to compare the CBF parameters between them using transcranial Doppler ultrasonography.

Patients and methods

Study design

This work was a cross-sectional study conducted on 40 smoker patients.

Study patients

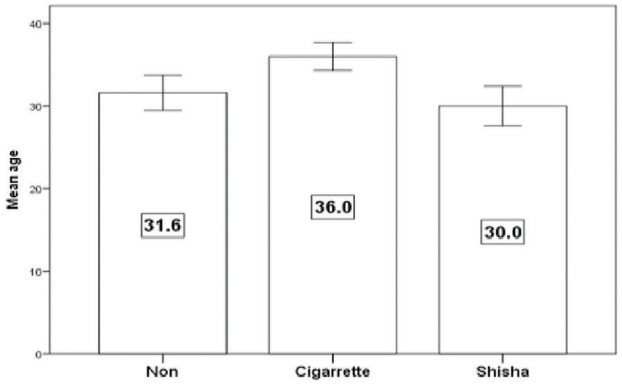
A total of 47 male smokers participated in this study. They were recruited from medical staff and their relatives in our University Hospitals from March 2019 through January 2020. Their ages were less than 40 years. Seven patients did not finish the study, where they did not keep their appointments. A total of 40 smokers completed the study and were evaluated, comprising 20 cigarette smokers and 20 water-pipe smokers. Moreover, 20 age-matched and sex-matched apparently healthy volunteers served as controls. The groups were age matched [Fig. 1].

Case selection

The patients' age ranged from 21 to 40 years, with a mean of 32.5±5.2 years.

(1) Inclusion criteria: patients were eligible for study if they were either cigarette or water-pipe smokers, and their ages were less than 40 years.
(2) Exclusion criteria: smoker patients who have the following criteria were excluded: (a) any medical

Figure 1



Age distribution of the studied cohort.

illnesses such as anemia, diabetes mellitus, hypertension, cardiac and/or chest problems, and hepatic/renal impairment or other systemic illnesses that could affect transcranial duplex (TCD) results; (b) any neurological diseases that affect CBF such as cerebrovascular diseases and/or insufficiency; (c) autoimmune diseases such as rheumatoid arthritis, systemic lupus erythematous, and scleroderma; (d) history of acute/chronic inflammatory diseases, trauma, surgery, or known diagnosis of vacuities; (e) malignancy elsewhere in the body or brain, and (f) a poor TCD acoustic temporal window.

Study tools: all patients were subjected to the following:

(1) Complete medical and neurological examination, where the following clinical and demographical data were taken: age, duration of smoking, number of cigarette and/or boxes smoked per day, and smoking index.
(2) Laboratory tests: it included (a) HBA1C, (b) complete liver and renal function test, (c) lipid profile, and (d) vacuities workup as erythrocyte sedimentation rate, and rheumatoid factor.
(3) Bilateral transcranial color coded duplex (TCCD) using ultrasound machine having 2–4 MHz phase array probe.

Description of the procedure

Participants were subjected to TCCD by using the available TCD apparatus (LOGIQ V5, Alkan Medical, GE-Ultrasound Solution [GE Healthcare, China]). Assessment of intracranial cerebral vasculatures was done through transtemporal and suboccipital bone windows by the technique described by Aaslid [4]. Peak systolic velocity (PSV), end diastolic velocity, and pulsatility index (PI) and resistivity index (RI) of middle cerebral (MCA), anterior cerebral (ACA), posterior cerebral artery (PCA), vertebral artery (VA) and basilar artery (BA) arteries were determined.

Ethical consideration

The study was approved by local institutional ethical committees, Faculty of Medicine of our University. Written informed consent was obtained from all participants. Approval for the study was obtained from the IRB committee of our Medical Faculty (No. of IRB: aswu/442/3/20). The study was conducted in accordance with the principles of Declaration of Helsinki.

Sample size calculation

Sample size calculation was carried out using G*Power 3 software [5]. A calculated minimum sample of 60 patients was needed. The sample was divided into three age-matched equal groups: 20 in group A, who were cigarette smokers; 20 in group B, who were shisha smokers; and 20 in group C, who were nonsmokers. The calculated sample was needed to detect an effect size of 0.2 in the mean cerebral vascular parameters, with an error probability of 0.05 and 80% power.

Statistical analysis

It was performed using IBM-SPSS version 21.0 (IBM-SPSS, Chicago, Illinois, USA). Data were presented as mean ± SD. Differences between groups for dichotomous variables were analyzed by independent *t* test. Moreover, differences between groups for variables with more than two categories were analyzed using analysis of variance, followed by post-hoc analysis with Bonferroni's test correction for normally distributed values. *P* value less than or equal to 0.05 was considered significant.

Results

Regarding MCA and ACA, there was a significant difference in the mean PSV, PI, and RI among the three groups ($P < 0.001$). Moreover, these parameters for shisha smokers were higher compared with cigarette smokers and nonsmokers ($P < 0.01$). Likewise, cigarette smokers reported significantly higher mean parameters than nonsmokers ($P < 0.001$), as shown in Table 1. Furthermore, regarding the posterior circulation, there was a significant difference in the mean PSV, PI, and RI among the three groups ($P < 0.001$). Moreover, mean PCA parameters for shisha and cigarette smokers were significantly higher compared with nonsmokers ($P < 0.01$). However, the results did not detect significant difference between two smoker groups ($P > 0.05$). In addition, mean VA and BA parameters for shisha smokers were significantly higher compared with cigarette smokers and nonsmokers ($P < 0.01$) [Table 2].

Table 1 Main transcranial color coded duplex parameters of anterior circulation in studied groups

Parameters	Nonsmoker (1) (*n*=20)	Cigarette smoker (2) (*n*=20)	Shisha smoker (3) (*n*=20)	*P**
Rt. MCA				
PSV	99.80±10.9	161.40±23.3	202.10±22.2	<0.001
P †	1 vs. 2<0.001	2 vs. 3<0.001	1 vs. 3<0.001	
PI	1.18±0.5	1.80±0.6	2.58±0.9	<0.001
P	1 vs. 2=0.008	2 vs. 3=0.001	1 vs. 3<0.001	
RI	0.76±0.2	1.24±0.4	1.59±0.3	<0.001
P	1 vs. 2<0.001	2 vs. 3=0.001	1 vs. 3<0.001	
Rt. ACA				
PSA	98.70±6.8	106.30±21.5	122.60±15.9	<0.001
P	1 vs. 2=0.136	2 vs. 3=0.002	1 vs. 3<0.001	
PI	1.16±0.5	1.77±1.0	2.27±0.7	<0.001
P	1 vs. 2=0.013	2 vs. 3=0.041	1 vs. 3<0.001	
RI	0.78±0.3	1.15±0.3	1.37±0.3	<0.001
P	1 vs. 2<0.001	2 vs. 3=0.022	1 vs. 3<0.001	
Lt. MCA				
PSA	98.70±9.6	155.50±41.3	181.90±24.8	<0.001
P value	1 vs. 2<0.001	2 vs. 3=0.005	1 vs. 3<0.001	
PI	1.11±0.4	1.63±0.8	1.89±0.5	<0.001
P	1 vs. 2=0.006	2 vs. 3=0.229	1 vs. 3<0.001	
RI	0.63±0.2	1.10±0.3	1.29±0.4	<0.001
P	1 vs. 2<0.001	2 vs. 3=0.066	1 vs. 3<0.001	
Lt. ACA				
PSA	92.10±19.2	120.70±16.5	127.50±7.5	<0.001
P	1 vs. 2<0.001	2 vs. 3=0.173	1 vs. 3<0.001	
PI	0.91±0.3	2.34±1.0	2.50±0.9	<0.001
P	1 vs. 2<0.001	2 vs. 3=0.541	1 vs. 3<0.001	
RI	0.60±0.3	1.02±0.3	1.23±0.3	<0.001
P	1 vs. 2<0.001	2 vs. 3=0.027	1 vs. 3<0.001	

ACA, anterior cerebral artery; Lt, left; MCA, middle cerebral artery; PI, pulsatility index; RI, resistivity index; Rt, right.*Analysis of variance test was used to compare the mean difference between groups.†Post-hoc test with Bonferroni correction; PSV, Peak systolic velocity

Heavy smokers are defined as those who smoke 20 or more cigarettes per day, or 20 or more pack-years according to Tchounwou and Han [6]. Our study revealed a nonstatistically significant difference among the groups regarding mean parameters of MCA, ACA, PCA, and right VA ($P > 0.05$). Nevertheless, PSV in the left VA and BA was significantly higher in those with severe smoking index (heavy smokers) compared with moderate smokers ($P < 0.05$), as shown in Tables 3 and 4.

Discussion

One interesting aspect of the association between smoking and cerebrovascular disorders is the fact that younger adults with the same number of pack-years as older adults seem to run a greater risk of cerebral infarction [7]. The present study evaluated tobacco and water pipe-related CBF and compared these changes between them using TCCD. We revealed significant difference in CBF parameters of the anterior and posterior circulations among the three groups. Moreover, these parameters were higher for shisha smokers compared with cigarette smokers and non-smokers. Likewise, cigarette smokers reported significantly higher mean parameters than nonsmokers. Both types of smoking had similar toxic effects, supporting what was concluded by Golbidi *et al.* [8], who reported that toxic substances in hookahs may act through a mechanism similar to that in cigarettes. Although global cerebral hypoperfusion has been proposed in our study, increased cerebrovascular reactivity was established. In our study, both RI and PI increased, indicating that cerebral arterial resistances and impedances are increased in smokers. These hemodynamic changes are believed to result from the elevated nicotine level, leading to an increase in norepinephrine, epinephrine, and vasopressin or through its direct effect on the endothelium and sympathetic nervous system activation. Chronic smoking leads to changes in brain physiology, such as an upregulation of nicotinic acetylcholine receptors [9]. Our results were in concordance with Song *et al.* [10] who reported that smoking results in decreases in the cerebral flow rate in the ACA, MCA, and PCAs, whereas our findings were inconsistent with Karakayalı *et al.* [2], who reported varying degrees of distal blood flow increases in intracranial vessels among patients who smoked water-pipe. However, the authors stated a decrease in both PI and RI. This discrepancy could

Table 2 Main transcranial color coded duplex parameters of posterior circulation in studied groups

Parameters	Nonsmoker (1) (*n*=20)	Cigarette smoker (2) (*n*=20)	Shisha smoker (3) (*n*=20)	*P**
Rt. PCA				
PSA	95.70±10.5	103.20±22.1	111.60±10.2	0.007
P †	1 vs. 2=0.127	2 vs. 3<0.088	1 vs. 3=0.002	
PI	0.96±0.2	2.09±0.6	2.14±0.6	<0.001
P	1 vs. 2<0.001	2 vs. 3=0.747	1 vs. 3<0.001	
RI	0.78±0.2	1.06±0.3	1.19±0.3	<0.001
P	1 vs. 2=0.004	2 vs. 3=0.200	1 vs. 3<0.001	
Rt. VA				
PSA	74.00±14.9	78.90±17.2	92.50±9.2	<0.001
P	1 vs. 2=0.284	2 vs. 3=0.004	1 vs. 3<0.001	
PI	0.91±0.4	1.12±0.7	1.18±0.8	0.404
P	1 vs. 2=0.322	2 vs. 3=0.768	1 vs. 3=0.200	
RI	0.54±0.2	0.62±0.2	0.72±0.2	0.012
P	1 vs. 2=0.192	2 vs. 3=0.086	1 vs. 3=0.003	
Lt. PCA				
PSA	83.10±12.8	116.60±15.1	118.60±12.5	<0.001
P	1 vs. 2<0.001	2 vs. 3=0.729	1 vs. 3<0.001	
PI	1.06±0.4	1.52±0.9	1.77±0.4	0.001
P	1 vs. 2=0.006	2 vs. 3=0.229	1 vs. 3<0.001	
RI	0.75±0.2	1.08±0.4	1.20±0.3	<0.001
P	1 vs. 2<0.002	2 vs. 3=0.269	1 vs. 3<0.001	
Lt. VA				
PSA	79.10±8.8	86.30±11.8	93.20±7.5	0.004
P	1 vs. 2<0.095	2 vs. 3=0.081	1 vs. 3=0.001	
PI	1.11±0.5	1.63±0.7	1.98±0.4	0.049
P	1 vs. 2=0.144	2 vs. 3=0.309	1 vs. 3=0.015	
RI	0.67±0.2	1.80±0.3	1.03±0.4	0.002
P	1 vs. 2=0.178	2 vs. 3=0.025	1 vs. 3=0.001	
BA				
PSA	80.80±14.2	101.80±10.4	107.40±11.8	<0.001
P	1 vs. 2<0.001	2 vs. 3=0.275	1 vs. 3<0.001	
PI	1.25±0.5	1.56±0.5	1.79±0.8	0.038
P	1 vs. 2=0.160	2 vs. 3=0.231	1 vs. 3=0.011	

BA, basilar artery; Lt, left; PCA, posterior cerebral artery; PI, pulsatility index; RI, resistivity index; Rt, right; VA, vertebral artery.*Analysis of variance test was used to compare the mean difference between groups.†Post-hoc test with Bonferroni corrections.

be explained by methodological cause, where they studied acute effects of smoking by evaluation of P1 and RI indices after 45 min of water-pipe smoking in closed area, where hypercapnia occurs leading to vascular relaxation and vasodilatation. Moreover, their study included the immediate effects of smoking that leads to reduced cardiac output by reducing peripheral cerebrovascular impedance and possibly promoting vasospasm of the MCA and/or other basal cerebral arteries. In this respect, Silvestrini *et al.* [11] reported reduced cerebrovascular reactivity to hypercapnia after smoking, which was found immediately after and at least 20 min after smoking. Rogers *et al.* [12] and Yamashita *et al.* [13] stated that long-term cigarette smoking has been shown to reduce rCBF, possibly by hypocapnia caused by small airway disturbances[12] or by impaired neurovascular coupling owing to structural changes in blood vessels [13]. Kodaira *et al.* [14] found that the increased MFV after smoking is associated with a reduction of the PI, so suggesting a dilatation of the small resistance vessels. However, other studies, in which the effects of smoking on cerebral hemodynamics were investigated using TCD and the 133Xe inhalation technique, did not confirm this effect such as Cruickshank *et al.* [15] and Dorrance and Dwyer [16]. Our study illustrated no significant effect of smoking severity on the vascular parameters among the smokers either heavy or moderate smokers. This supported what is stated by Kubota *et al.* [17] which found significantly and equally low CBF values for the smokers in all groups that separated according to their smoking indices, from 1 to 200, and more than 200 compared with those of nonsmokers. This indicates that smoking effect has no relation to the severity of smoking. However, our results are inconsistent with findings of Durazzo *et al.* [18] who reported that moderate-strength associations between greater lifetime years of smoking (age-adjusted) decreased perfusion levels in smokers. Moreover, Elbejjani *et al.* [19] conveyed that among current-smokers, higher pack-years were associated with higher CBF. This discrepancy could be explained by their method

used to measure CBF, where structural (T1, T2, and FLAIR), and arterial spin labeling magnetic resonance studies were used.

Conclusion

In conclusion, our study reported that cigarette and water-pipe smoking status were associated with changes in CBF, an important early indicator of

Table 3 Effect of smoking severity on the cerebral blood flow parameters of anterior circulation in studied groups

Parameters	Moderate (*n*=18)	Severe (*n*=22)	*P**
Rt. MCA			
PSV	180.11±31.0	183.09±30.3	0.763
PI	2.04±1.0	2.31±0.7	0.341
RI	1.41±0.3	1.42±0.4	0.909
Lt. MCA			
PSV	166.44±34.1	170.55±31.3	0.725
PI	1.73±0.6	1.74±0.7	0.959
RI	1.28±0.5	1.12±0.2	0.162
Rt. ACA			
PSV	115.11±21.7	113.91±19.6	0.856
PI	1.74±0.7	1.24±0.9	0.065
RI	1.30±0.3	1.22±0.3	0.414
Lt. ACA			
PSV	122.89±10.5	125.09±15.1	0.529
PI	2.36±0.6	2.47±1.2	0.712
RI	1.24 ± 0.3	1.03 ± 0.3	0.027

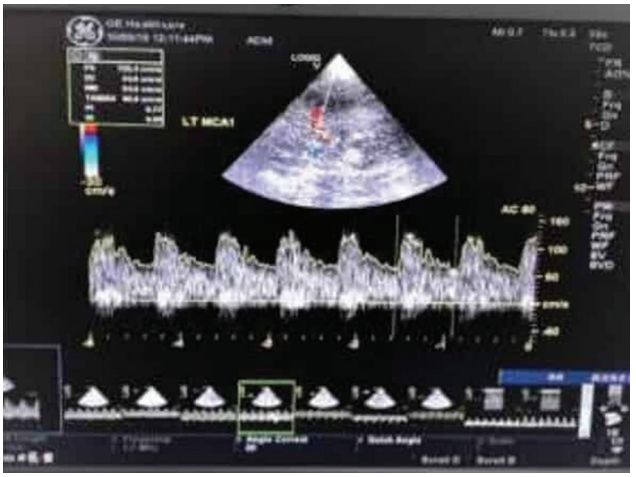
ACA, anterior cerebral artery; Lt, left; MCA, middle cerebral artery; PI, pulsatility index; PSV, peak systolic velocity; RI, resistivity index; Rt, right.*Independent *t* test was used to compare the mean difference between groups.

Table 4 Effect of smoking severity on the cerebral blood flow parameters of posterior circulation in studied groups

Parameters	Moderate (*n*=18)	Severe (*n*=22)	*P**
Rt. PCA			
PSV	106.67±19.0	108.00±16.6	0.814
PI	2.02±0.5	2.18±0.6	0.370
RI	1.09±0.3	1.15±0.3	0.595
Lt. PCA			
PSV	116.78±14.6	118.27±15.9	0.818
PI	1.43±0.5	1.82±0.8	0.061
RI	1.25±0.3	1.05±0.4	0.074
Rt. VA			
PSV	87.78±9.9	84.00±10.3	0.324
PI	1.12±0.6	1.17±0.9	0.822
RI	0.67±0.2	0.68±0.2	0.730
Lt. VA			
PSV	83.56±11.3	94.82±9.2	0.009
PI	2.02±0.5	1.48±0.1	0.074
RI	1.09±0.3	0.82±0.3	0.057
BA			
PSV	99.00±13.7	109.18±11.6	0.034
PI	1.59±0.8	1.74±0.6	0.517
RI	0.86 ± 0.4	0.85 ± 0.3	0.927

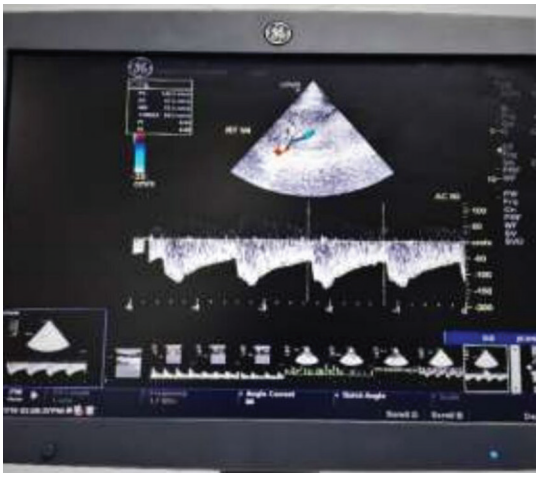
BA, basilar artery; Lt, left; PCA, posterior cerebral artery; PI, pulsatility index; PSV, peak systolic velocity; RI, resistivity index; Rt, right; VA, vertebral artery.*Independent *t* test was used to compare the mean difference between groups.

Figure 2



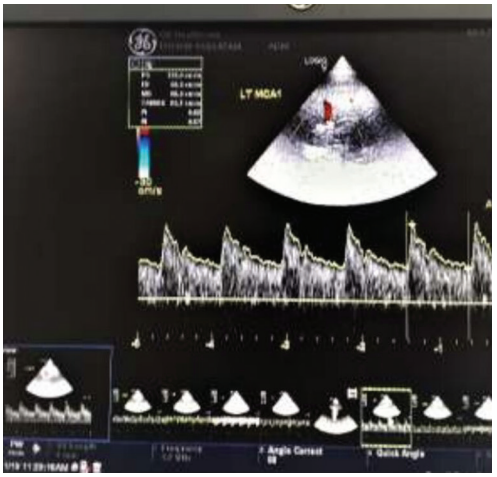
TCCD of water-pipe smoker shows increased PSV and PI of MCA. MCA, middle cerebral artery; PI, pulsatility index; PSV, Peak systolic velocity; TCCD, transcranial color coded duplex.

Figure 3



TCCD of water-pipe smoker shows increased PSV of left vertebral artery (intracranial part). PSV, peak systolic velocity; TCCD, transcranial color coded duplex.

Figure 4



TCCD of cigarette smoker shows increased PSV of MCA. MCA, middle cerebral artery; PSV, Peak systolic velocity; TCCD, transcranial color coded duplex.

cerebrovascular pathology. Longitudinal investigations are needed to identify how and when the patterns of cerebral blood perfusion change with changes in smoking status throughout the lifespan.

Study strength and limitation

To our best knowledge, this is the first functional TCD study in our country that compared cigarette and water-pipe smoking effects on CBF. The limitation of the present study is the involvement of limited number of shisha smokers because most of the people use both shisha and cigarette and we selected only male shisha smokers (Figures 2–4).

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Conflicts of interest

There are no conflicts of interest.

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