The long-term effects of hypobaric and hyperbaric conditions on brain hemodynamic: A transcranial Doppler ultrasonography of blood flow velocity of middle cerebral and basilar arteries in pilots and divers

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KEYWORDS
Hypobaric condition; Hyperbaric condition; Brain hemodynamic; Transcranial Doppler ultrasonography; Blood flow velocity

Summary
Background: Nowadays, more attention is paid to the potential risk factors of cerebrovascular events including some environmental conditions. We aimed to compare the long-term effects of hypobaric condition of pilots versus hyperbaric condition of divers as two possible occupational risk factors on blood flow velocity of middle cerebral and basilar arteries.

Methods: This cross-sectional study was performed in Firoozgar Hospital, Tehran, Iran between March 2009 and June 2010. A final number of 15 pilots and 16 divers were referred to the Neurology Laboratory of Firoozgar Hospital. Afterward, Transcranial Doppler ultrasonography was performed to evaluate blood flow velocity of middle cerebral (MCA) and basilar arteries.

Results: Comparison of the TCD findings between these two groups showed that resistance index was significantly higher in divers [0.57 (SD = 0.03) vs. 0.52 (SD = 0.06), \( P = 0.008 \)]. A significant inverse correlation was also found between total working index of the pilots and the mean velocities (\( r = -0.58, P = 0.027 \)) of right MCA even after eliminating the confounding effect of age.

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Introduction

With an annual incidence of about 795,000 in the United States [1], and a various incidence rate of 8–43.2 per 100,000 in Iran [2,3], stroke is a highly burdened disease [4] which is estimated to cause 5.7 million deaths in the year 2004 worldwide [5]. As a global considerable problem, much attention is currently paid to the potential risk factors of stroke. Although the previous well-known risk factors (e.g. hypertension, current smoking, diabetes mellitus, alcohol intake, depression, psychosocial, and lack of regular physical activity) were recently confirmed in a multicenter case–control study [6], more attempts are made to find out other probable risk factors.

Some evidence proposed hypobaric environment as a potential risk factor for cerebrovascular events. In a review by Clarke it was concluded that stroke and transient ischemic attack (TIA) occur more frequently than one might expect at high altitudes [7]. Another review by Wilson also revealed a considerable incidence of brain edema and headache following cerebral blood flow disturbance and cellular hypoxia induced by ascent to high altitudes [8]. Moreover, the experiences of TIA are reported in some cases of pilots [9,10].

On the other hand, hyperbaric condition of divers is also thought to be associated with a higher incidence of cerebral ischemic events [11–14]. Even though patent foramen ovale (PFO) is mostly introduced to be accompanied with these attacks, a recent study confirms the association between hyperbaric condition and cerebral ischemic events regardless of PFO [13].

Being exposed to long-term hypobaric and hyperbaric environments, pilotage and diving might be considered as occupational risk factors for brain ischemic events and consequent stroke. According to the literature review, most of the previous studies either have indirectly evaluated this relationship in artificial situation of high altitudes or reported only a limited number of cases of pilots. Furthermore, none of them have addressed the comparison between hypobaric and hyperbaric effects on brain hemodynamic. Thus, our study was designed to perform this comparison between pilots and divers. We aimed to evaluate the long-term effects of hypo/hyperbaric conditions on flow velocity of middle cerebral and basilar arteries by means of Transcranial Doppler (TCD) ultrasonography.

Methods and subjects

Individual enrollment

This cross-sectional study was performed in Firoozgar Hospital affiliated to Tehran University of Medical Sciences (TUMS), Tehran, Iran between March 2009 and June 2010. The study protocol was approved by research committee of both Tehran University of Medical Sciences (TUMS) and AJA University of Medical Sciences. Moreover, a verbal consent form was taken from all the recruited cases. All the eligible persons had at least 2 years of working history without any previous history of cerebrovascular or cardiovascular events. Finally, a total number of 15 pilots and 16 divers were selected by snowball sampling method and referred to the Neurology Laboratory of Firoozgar Hospital.

Blood flow velocity measurements

After recruitment, Transcranial Doppler (TCD) ultrasonography was performed to evaluate blood flow velocity of middle cerebral (MCA) and basilar arteries for all of the cases. All the TCD measurements were performed by the same two experienced neurologists. Cerebral blood flow was estimated by a 2MHz Transcranial Doppler ultrasound probe (Transcranial Doppler, Esaote, Genoa, Italy) fixed over temporal window to insonate the proximal segment of middle cerebral artery (MCA). Also in order to assess basilar artery, foramen magnum window was used. Once the optimal signal-to-noise ratio was obtained, the probe was covered with an adhesive ultrasonic gel and secured with a headband device (Multigon) to maintain optimal insonation position and angle throughout the protocol. Optimization of the Doppler signals from the MCA and basilar artery was performed by varying the sample volume depth in incremental steps and at each depth, varying the angle of insonance to obtain the best-quality signals from the Doppler frequency. In addition to basilar artery, both right and left MCAs’ velocities were monitored reporting the main indexes including peak systolic velocity, end diastolic velocity and mean flow velocities. Consequently, other indexes such as systolic/diastolic velocity ratio, pulsatility index (PI) and resistance index (RI) were calculated using following formulas [15]:

$$PI = \frac{V_{\text{peak systolic}} - V_{\text{end diastolic}}}{V_{\text{mean}}}$$

$$RI = \frac{V_{\text{peak systolic}} - V_{\text{end diastolic}}}{V_{\text{peak systolic}}}$$

In addition to flow velocity indexes, baseline characteristics (e.g. smoking history, family history of cerebrovascular diseases, diabetes mellitus, and hypertension), laboratory variables (e.g. liver function test, lipid profile, blood sugar) and occupational indexes (duration of working, height or depth of working, working hours per week) were also recorded for each person.
**Statistical analysis**

Qualitative and quantitative variables were described by frequency percentages, mean and standard deviation (SD), respectively. Univariate comparisons were performed using independent sample t-test and Mann–Whitney U-test. Afterwards, analysis of covariance (ANCOVA) and partial correlation methods were used to adjust the comparisons by controlling for confounders in multivariate procedures. All the analytical processes were performed by SPSS v.16 software (Chicago, IL, USA). A P-value less than 0.05 was considered to be statistically significant.

**Results**

A total of 15 pilots and 16 divers aged 21–60 years participated in this study. All participants were male with a mean work history of 21 (SD = 12.53) years. None of demographic, baseline and laboratory characteristics were significantly different in two groups except for age (P < 0.001) and work history (P = 0.004).

TCD findings of right and left MCA and basilar artery were compared between two groups of this study, pilots and divers. Resistance index, pulsatility index and systolic to diastolic velocity ratio of right MCA were all significantly lower in pilots in comparison with divers (P = 0.008 and 0.045 and 0.021, respectively). However, speed values including mean flow velocities and end diastolic velocities were not statistically different in bivariate analysis (Tables 1–3).

Considering the age as a confounder of comparisons, a set of statistical methods employed for eliminating its effect. Analysis of covariance (ANCOVA) for controlling the variable age, revealed a significantly higher mean flow velocity of 44.09 (±2.48) cm/s versus 35.74 (±2.48) cm/s of divers (P = 0.040). A similar difference was found between end diastolic velocity of this artery in these two groups; pilots with adjusted mean of 32.30 (±1.85) cm/s were significantly different from divers with adjusted mean of 25.02 (±1.85) cm/s (P = 0.018). By controlling the effect of age with partial correlation analysis, a significant reverse correlation was also detected between index of total working and mean flow velocity of right MCA in pilots (r = −0.58, P = 0.027).

**Discussion**

Little is known about the effect of hypobaric and hyperbaric condition on brain hemodynamic in pilots and divers according to literature review. Our study was performed to assess and compare blood flow velocity indexes between pilots and divers as representatives of hypobaric and hyperbaric conditions. While trying to explore these new features in cerebral investigations, some novel findings were expected to be revealed.

In this study, with controlling the effect of age, divers appeared to have lower flow velocities including peak systolic and end diastolic as well as mean flow velocity. On the other hand, divers have also a significantly higher resistance index (RI) and pulsatility index (PI) which is in favor of low stage atherosclerotic changes of brain arteries. Although the divers were significantly younger than the pilots, these hemodynamic findings remained or even strengthened after adjusting the age effect between two study groups. These results were more significant in the right MCA which is mostly considered artery for brain hemodynamic studies in previous researches where they have shown no systematic differences in MCA flow velocities measured from the right or left sides by use of similar methodology [16,17].

Considering the normal range of PI between 0.6 and 1.1 [18], most of the cases have values within the normal range. However, a PI of lower than 0.6 (stenosis) was detected in the basilar artery of four individuals which all belonged to divers’ group (25% vs. none, P < 0.05). Furthermore, another 2 divers had a PI of higher than 1.1 which is in favor of attenuated blood flow in basilar artery. In pilots’ group, the entire measured PI’s were found to be within the normal range despite the significantly higher mean age in this group.

**Table 1** Comparison of TCD findings of right MCA between pilots and divers.

<table>
<thead>
<tr>
<th>Velocity index</th>
<th>Unadjusted values</th>
<th>Adjusted values</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Groups of study</strong></td>
<td><strong>P-value</strong></td>
<td><strong>Groups of study</strong></td>
</tr>
<tr>
<td><strong>Pilots</strong> (n = 15)</td>
<td><strong>Divers</strong> (n = 16)</td>
<td><strong>Pilots</strong> (n = 15)</td>
</tr>
<tr>
<td><strong>Peak systolic velocity (cm/s)</strong></td>
<td>63.67 ± 16.12</td>
<td>61.20 ± 13.07</td>
</tr>
<tr>
<td>Range</td>
<td>41–90</td>
<td>41–92</td>
</tr>
<tr>
<td><strong>End diastolic velocity (cm/s)</strong></td>
<td>30.53 ± 7.72</td>
<td>26.80 ± 5.57</td>
</tr>
<tr>
<td>Range</td>
<td>20–45</td>
<td>21–41</td>
</tr>
<tr>
<td><strong>Mean flow velocity (cm/s)</strong></td>
<td>41.58 ± 10.13</td>
<td>38.27 ± 7.89</td>
</tr>
<tr>
<td>Range</td>
<td>27.00–58.67</td>
<td>29.67–58.00</td>
</tr>
<tr>
<td><strong>Systolic/diastolic velocity ratio</strong></td>
<td>2.11 ± 0.25</td>
<td>2.32 ± 0.23</td>
</tr>
<tr>
<td>Range</td>
<td>1.56–2.55</td>
<td>1.71–2.71</td>
</tr>
<tr>
<td><strong>Resistance index</strong></td>
<td>0.52 ± 0.06</td>
<td>0.57 ± 0.03</td>
</tr>
<tr>
<td>Range</td>
<td>0.36–0.61</td>
<td>0.53–0.63</td>
</tr>
<tr>
<td><strong>Pulsatility index</strong></td>
<td>0.80 ± 0.14</td>
<td>0.90 ± 0.12</td>
</tr>
<tr>
<td>Range</td>
<td>0.47–1.02</td>
<td>0.57–1.07</td>
</tr>
</tbody>
</table>

* Statistical significant difference (P < 0.05).
These findings could probably emphasize the potential harmful role of hyperbaric working situation of divers compared with hypobaric environment of pilots.

A previous study by Boussuges et al. [19] showed numerous hemodynamic changes after an open-sea scuba dive. Although they have investigated hemodynamic changes after 1 h post-diving, an increase in heart rate and decrease in systolic flow velocity were demonstrated. Afterwards, they proposed two possible factors to explain these hemodynamic alterations including low volemia secondary to immersion, and venous gas embolism induced by nitrogen desaturation occurred in divers [19]. Another recent study by Moen et al. [20] that was performed on Norwegian professional divers shows widespread diffusion and perfusion abnormalities in different parts of brain hemodynamic of divers compared with controls. They concluded that several mechanisms could be contributing differently in various regions, depending for instance on the brain vessel size [20]. Compared to these previous studies, our samples of professional divers were younger in age and it is very important to show these brain hemodynamic changes in an age-group where it is not expected to have senile atherosclerotic changes yet.

Not only have they been evaluated in brain hemodynamics, but also there are some previous evidence which show that some other brain damages are more prevalent in divers including abnormalities of the electroencephalogram (EEG) [21,22] and even impaired function in some cognitive domains [23,24].

By contrast to the divers, no brain hemodynamic abnormality was detected within pilots’ group. Even though the pilots were significantly more aged than the divers, measured flow velocities were higher and the mean RI and PI were lower which are in favor of a better brain hemodynamic. It must be noted that the other well-known risk factors for cerebrovascular events such as lipid profile, family history of stroke, myocardial infarction, diabetes mellitus, hypertension, and smoking history were not significantly different between two groups of study. However,
after controlling for age, still a significant reverse correlation was also detected between index of total working and mean flow velocity of right MCA in pilots demonstrating that the higher the working duration and height of pilotage are, the lower flow velocities are expected which could be explained by hopoxic hypobaric effects of their working condition. Although not as strong as the divers, this association may be implied as the effect of pilots’ chronic hypobaric condition.

Although our study has some limitations including cross-sectional design and small sample size, it must be taken into account that our TCD findings could explain some of the long-term clinical symptoms commonly reported among professional divers. In conclusion, chronic exposure to the hyperbaric condition of diving seems to have some probable effects on brain hemodynamics in the long-term which are in favor of decreasing blood flow and increasing of RI and PI. It is strongly recommended to evaluate the changes of brain hemodynamics in this working group (diving) by performing some longitudinal studies assessing the alteration of TCD indexes over the time in divers.

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