Effect of helium on cerebral blood flow: A \( n = 1 \) trial in a healthy young person

Sanne M. Zinkstok\(^a\), Daniela Bertens\(^b\), Jelle R. de Kruijk\(^c\), Selma C. Tromp\(^d,\ast\)

\(^a\) Department of Neurology, Academic Medical Center, University of Amsterdam, PO Box 22660, 1100 DD Amsterdam, The Netherlands
\(^b\) Department of Neurology, VU University Medical Center, De Boelelaan 1117, 1081 HV Amsterdam, The Netherlands
\(^c\) Department of Neurology, Tergooiziekenhuizen, Rijksstraatweg 1, 1261 AN Blaricum, The Netherlands
\(^d\) Department of Clinical Neurophysiology, St. Antonius Hospital, PO Box 2500, 3430 EM Nieuwegein, The Netherlands

**KEYWORDS**
- Transcranial Doppler;
- Helium;
- Heliox

**Summary**  Several experimental studies have shown that noble gases can have neuroprotective effects in cerebral ischemia. The exact mechanism is unknown; increased cerebral blood flow may play a role. In order to investigate this concept we performed a \( n = 1 \) trial measuring cerebral blood flow velocity by means of transcranial Doppler (TCD) in a healthy young woman inhaling air or heliox. Peak systolic velocity, mean flow velocity and pulsatility index were measured in the right middle cerebral artery, and oxygen saturation and heart rate were measured with pulse oximetry. After a baseline of 3 min breathing normal air, heliox (79% helium, 21% oxygen) was inhaled though an oral nasal mask for 5 min, followed by a washout period of 5 min breathing normal air. This protocol was repeated four times. No significant changes were observed in hemodynamic parameters, except for a small increase in pulsatility index during heliox inhalation (from 0.91 to 0.95; \( p = 0.01 \)).

In conclusion, inhalation of heliox does not influence cerebral blood flow in a healthy young person. Any beneficial effects of helium in stroke patients are more likely due to other neuroprotective effects than to hemodynamic changes.

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**Introduction**

Given the narrow therapeutic time window for reperfusion in acute ischemic stroke, there is a strong need for neuroprotective strategies aiming at preservation of tissue at risk for infarction to increase the number of patients eligible for reperfusion. Former clinical trials in neuroprotection led to disappointing results due to poor interpretation and translation from an experimental to a clinical setting.

When selecting agents for neuroprotection not only proof of efficacy but also easy implementation in acute stroke care is of great importance. Gas therapy and especially the noble gas helium might be a promising neuroprotective strategy that meets criteria for every day practical use \([1–3]\). Helium is directly available in the hyperacute prehospital phase, is well-tolerated and lacks toxicity or interactions \([4,5]\). The exact neuroprotective mechanism of helium is not well known but egression of nitrogen from neural mitochondria is suggested. This might facilitate oxygen reuptake during...
reperfusion [6]. Another supposed mechanism of neuroprotection by gas therapy is an increase of cerebral blood flow. Rats with distal middle cerebral artery occlusion breathing 100% oxygen had an increase in cerebral blood flow (CBF), while infarct size was decreased compared to rats breathing 30% oxygen. Since the concentration of oxyhemoglobin in the infarct core was increased in the 100% oxygen group, a better tissue delivery of oxygen due to a higher CBF might explain the results [7]. On the other hand, increased blood flow might cause reperfusion damage or hypertensive hemorrhage in the infarction area during reperfusion.

Before studying any neuroprotective effect of helium in acute ischemic stroke in humans, it is necessary to know if helium influences cerebral blood flow in healthy people. In order to investigate this, we performed a n = 1 trial measuring cerebral blood flow parameters by means of transcranial Doppler (TCD) in a healthy young women alternatingly inhalating air or helium.

**Methods**

To measure cerebral blood flow TCD was performed with a pulsed Doppler transducer (Pioneer TC4040, EME Überlingen, Germany), gated at a focal depth of 50 mm. Our female 29-year-old healthy volunteer was positioned laying on the back and the transducer (2 MHz) was placed at the right temporal bone. When the main stem of the right middle cerebral artery was found, the transducer was fixed with a head strap. The mean flow velocity (MFV), peak systolic velocity (PSV), and pulsatility index (PI) were measured continuously and recorded every minute. Furthermore, heart rate frequency and blood oxygen saturation were measured with a fingertip monitor (pulse oximetry) in order to exclude possible confounding factors.

At baseline all parameters were measured during 3 min while breathing normal room air. After baseline measurement, Heliox (helium 79%, oxygen 21%) was administrated for 5 min using an oral nasal mask. This intervention was followed by a washout of 5 min breathing room air. This block of 5 min Heliox intervention and 5 min washout was repeated four times. At the end, all measurements were performed during another period of 5 min breathing room air.

The null hypothesis was that there would not be any difference in the hemodynamic parameters during helium inhalation or room air inhalation. For analysis we used a one tailed Student’s t-test. We considered a P-value of less than 0.05 as statistically significant.

**Results**

No adverse events occurred during helium administration except for temporary changes in voice pitch. Median baseline values were: MFV 50 cm/s, PSV 79 cm/s, PI 0.92, heart rate 77 min⁻¹ and oxygen saturation 99%. Heart rate frequency and blood oxygen saturation were stable and did not differ significantly between the periods of breathing helium and room air. MFV in the right middle cerebral artery as well as the PSV did also not differ significantly in the two test conditions (Table 1).

The PI had a mean of 0.95 in Heliox compared to 0.91 in room air inhalation; this difference was significant with a P-value of 0.01.

**Discussion**

The present study investigated the effect of helium inhalation on cerebral blood flow in a healthy young person. We found that inhalation of helium did not influence cerebral blood flow as compared to inhalation of room air. The mean flow velocity and peak systolic velocity in the right middle cerebral artery as well as heart rate frequency and blood oxygen saturation did not differ during helium or room air (washout) inhalation.

Although the pulsatility index (PI) was significantly higher during helium inhalation, this effect was only small (0.95 versus 0.91), and the values stayed well within the normal range (0.6—1.1). A rise in PI can have different causes, such as a rise in intracranial pressure with reduced vessel compliance, bradycardia or hyperventilation. In our study the latter two did not contribute to the changes in PI, since heart rate frequency, blood oxygen saturation and cerebral blood flow did not change. Increased intracranial pressure has not been described after inhalation of a mixture of helium and oxygen before, although it has been widely used in pulmonary diseases. In addition, another noble gas xenon has been shown not to have any effect on intracranial pressure [8]. Therefore, increased intracranial pressure is not likely to be the cause of the minimal increase in PI.

In accordance to our findings, Pan et al. [3] did not find any significant differences in hemodynamic parameters in animals breathing helium as compared to animals breathing normal air. The present study confirms these findings in a healthy human being.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Results of the measurements in the two conditions.</th>
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<tbody>
<tr>
<td></td>
<td>Heliox</td>
</tr>
<tr>
<td>MFV (cm/s)</td>
<td>48.5 ± 3.4</td>
</tr>
<tr>
<td>PSV (cm/s)</td>
<td>77.0 ± 5.7</td>
</tr>
<tr>
<td>PI</td>
<td>0.95 ± 0.07</td>
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<tr>
<td>Oxygen saturation (%)</td>
<td>98.96 ± 0.35</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>77.6 ± 5.8</td>
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</tbody>
</table>

MFV = mean flow velocity; PSV = peak systolic velocity; PI = pulsatility index. Means and standard deviations are given.
Conclusions

Inhalation of helium does not influence cerebral blood flow in a healthy young person. If proven in future, beneficial effects of helium in stroke patients will be more likely due to other neuroprotective effects than to hemodynamic changes.

References


