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CO_2 Reactivity in Patients after Subarachnoid Haemorrhage

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Summary

CO_2 reactivity was tested in patients with transcranial Doppler sonography (TCD) and endtidal CO_2 measurements after an average time interval of ten months after subarachnoid haemorrhage (SAH). After deliberately changing breathing there was a significant change in endtidal CO_2 and in flow velocities in all three examination groups. Comparing 27 patients with SAH and 5 patients treated for incidential aneurysms and 20 patients without cerebrovascular disease there were no significant differences in CO_2 reactivity. Furthermore, there were no right to left differences. In 12 patients with vasospasm, two of them treated by percutaneous transluminal angioplasty for delayed ischaemic deficits, CO_2 reactivity was normal at the time of investigation. Furthermore, normal CO_2 reactivity was found in patients after SAH and surgery for ruptured aneurysms regardless of the severity of the SAH.

Keywords: CO_2 reactivity; transcranial Doppler sonography; subarachnoid haemorrhage; aneurysm surgery.

Introduction

Experimental studies on cerebral perfusion have proved that there is a linear correlation between changes in arterial CO_2 and cerebral blood flow (CBF) [3, 9, 12, 15, 18, 22]. In various cases of cerebrovascular disease CO_2 reactivity is impaired [5, 10, 11, 19]. TCD in combination with manipulations of cerebral resistance vessels using alterations of CO_2 is often used to assess the severity of cerebrovascular disease [4, 5, 6, 10, 11, 23, 24]. In the acute phase after SAH an impairment of CO_2 reactivity has been demonstrated [8, 17]. The aim of this study was to examine patients after SAH during long-term follow-up using alterations of CO_2 with TCD registrations of flow velocities to see whether disturbances of the CO_2 reactivity are detectable.

Methods and Patients

27 patients treated for ruptured aneurysm were entered into this study. The clinical neurological status on admission was judged using the Hunt and Hess scale [13]. The amount of blood in the subarachnoid space on the initial CT scan was graded according to the Fisher scale [7]. Outcome was classified using the Glasgow outcome scale (GOS) on discharge and at follow-up [14]. All patients had surgery to clip the aneurysm prior to the examination undertaken some (mean) 314.5 days (100–677 days) after the operation. Exclusion criteria were an absent temporal bone window and serious mental or neurological deficits. After assessment of the neurological status all cerebral vessels were insonated with the Multi Dop X (DWL-electronics, Sipplingen, Germany). The middle cerebral artery on both sides was then continuously insonated using a special fixation device while the patient was lying in supine position and resting. Endtidal CO_2 concentration was registered with a Datex normacap (Datex-electronics, Hoyer, Bremen, Germany). The detector was placed on top of a mask which was attached to the patient's head. After ten minutes a steady state of flow velocities and CO_2 values was reached and the mean flow velocity (MFV) was recorded. Following the registration patients were asked to deliberately hyperventilate to induce hypocapnia. MFV and CO_2 were recorded during the steady state. In a final step patients were asked to hypoventilate to induce hypercapnia and MFV and CO_2 were again recorded.

One control group consisted of 5 patients undergoing surgery for incidential aneurysms. 20 patients without cerebrovascular disease formed the second control group. Both groups were evaluated using the same investigational protocol as in the group of patients with ruptured aneurysms.

CO_2 reactivity was calculated using the equations proposed by Hartl [10] as shown in Table 1. The differences between the groups of patients were calculated using the student's T-test ($p < 0.05$). Furthermore, side-to side differences were calculated and correlated to the side of the aneurysm, the side of the surgical approach and/or the presence of vasospasm.

Table 1. *Equation to Calculate Absolute and Relative CO_2 Reactivity*

RV mean (absolute) = (Vmean hyper-Vmean hypo) / Δ CO_2
RV mean (relative) = R%Vmean = RVmean / Vmean hypo

Vmean mean blood flow velocity, *RVmean* absolute reactivity Vmean, *R%Vmean* relative reactivity Vmean.

Results

27 patients (25 females and 2 males) treated for ruptured aneurysms with a mean age of 44 years (range 13–69 years) formed one group. The majority of patients were Hunt and Hess II or III, Fisher grade II or III on admission as shown in Table 2. In one control group 5 patients were entered with surgery for incidential aneurysms with a mean age of 56.6 years. The second control group consisted of 20 volunteers (8 females and 12 males) with a mean age of 39.7 years (range 16–63 years) without cerebrovascular disorders. In all patients (n = 52) flow velocities of the vessels that could be insonated were within normal ranges. Especially in those patients after SAH and in patients who had developed vasospasm after surgery (n = 12) there were no persistant flow abnormalities present.

12 patients developed vasospasm (blood flow velocities > 120 cm/sec) during the postoperative course. Delayed ischaemic deficits were present in two patients due to critical vasospasm. Both patients had percutaneous transluminal angioplasty which improved the neurological deficits.

On discharge most patients were GOS 5. 5 patients, 4 with surgery for ruptured aneurysms and one with surgery for an incidential middle cerebral artery aneurysm, had partial infarction of the middle cerebral artery territory visible on postoperative CT scan. At follow-up the neurological status had improved as shown in Table 2.

Table 2. *Neurological Status, Amount of SAH and Outcome in Patients (n = 27) with SAH and Surgery for Ruptured Aneurysms*

H.-H.	n	Fisher	n	GOS	discharge	follow-up
I	4	1	3	5	16	25
II	10	2	12	4	9	2
III	8	3	12	3	2	0
IV	5	4	0	2	0	0
				1	0	0

Hunt and Hess scale (11), Fisher grading (5) on admission; the GOS (12) on discharge from our department and at follow-up investigation.

Table 3. *Changes in Endtidal CO_2 and Flow Velocities Induced in the Three Groups of Patients*

	Δ CO_2	Δ Vmean
Ruptured aneurysm (n = 27)	12.7 mmHg	30.1 cm/sec
Incidential aneurysm (n = 5)	13.2 mmHg	28.2 cm/sec
Control group (n = 20)	17.8 mmHG	33.1 cm/sec

The mean changes in CO_2 and in flow velocities registered in the three groups during the investigation are shown in Table 3. Δ CO_2 was higher in the control group than in the two groups of patients with aneurysms but the difference was not significant. ΔV mean was similar in all three groups.

CO_2 reactivity was normal in all patients treated for incidential aneurysms. There were no right-left differences with regard to the surgical approach detectable. In those patients (n = 20) without cerebrovascular diseases CO_2 reactivity was normal. Comparing the two control groups no significant differences were seen.

All patients (n = 27) with ruptured aneurysm, including the 12 patients with vasospasm had a normal CO_2 reactivity and there were no differences between patients with and without vasospasm. Furthermore, there were no differences between the side of the aneurysm or the side of the surgical approach and the other side detectable.

Comparing patients with severe SAH (H.–H. III, IV; F. III) and patients with mild SAH (H.–H. I, II; F. I, II) no significant differences were found.

Correlating the results of the control group with the group of patients with ruptured aneurysms there were no significant differences.

Regarding the time elapsed after SAH and the aneurysm surgery there were no differences between the patients evaluated 3–5 months after surgery and those investigated more than 1.5 years after surgery.

In seven of all patients with aneurysm surgery (n = 32) we compared the CO_2 reactivity which was tested during the operation [17] with the results obtained at this later investigation. 5 patients displayed a normal CO_2 reactivity in both examinations, whereas 2 patients had a disturbed CO_2 reactivity during the operation which was normal at the follow-up examination.

Discussion

In the acute phase after SAH, disturbances of CO_2 reactivity have been demonstrated [1, 2, 16, 17, 21]. The disturbance is more pronounced in patients graded Hunt and Hess III–IV and can be detected in patients developing vasospasm after SAH [1, 2, 16, 21]. In the case of a permanent impairment the outcome is poor [1, 2, 16]. Furthermore, an impairment

of CO_2 reactivity correlates well with the severity of cerebrovascular disease. In good agreement with other investigators we encountered a significant change in flow velocities following changes of endtidal CO_2. Even though the changes in CO_2 were more pronounced in the control group, the difference between the group of patients with ruptured aneurysms was not significant and changes in flow velocities were similar thus excluding a bias [6, 11, 19]. The changes in CO_2 and flow velocities induced by deliberately altering breathing patterns are pronounced enough to allow the testing of CO_2 reactivity without the use of gas mixtures with CO_2 as used in other studies [10, 19]

In this study all patients treated for ruptured aneurysms showed a normal CO_2 reactivity. Vasospasm in the postoperative course had no influence. Similar results were found by Seiler and Nirkko [21] at a two-month follow-up in patients with vasospasm after surgery for ruptured aneurysms. These results suggest that the disturbance of CO_2 reactivity if present after acute SAH does not persist long after surgery. Apart from that, one may conclude that the alterations of the cerebrovascular system after SAH, even a critical vasospasm is not severe enough to permanently impair the structures within the vascular bed responsible for CO_2 reactivity. It has to be kept in mind that whereas the neurological status on admission was representative for patients with SAH, at follow-up examinations only patients GOS 4 or 5 were investigated. This was mainly due to the fact that the investigational proceedings based on the cooperation of the patient excluded patients severely disabled or in a vegetative state. Aneurysm surgery had no influence on CO_2 reactivity with regard to hemispheric differences or differences between patients treated for ruptured or incidential aneurysms.

Conclusion

In a mean time interval of 10 months after SAH and surgery for ruptured aneurysms CO_2 reactivity is normal in patients with good outcome or moderate disabilities regardless of the severity of the SAH and/or the presence of vasospasm during postoperative course.

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Comments

The authors examine the CO_2 reactivity of patients with subarachnoid haemorrhage 10 months after the haemorrhage and compare it with patients who were treated for unruptured aneurysms or without cerebrovascular disease. They use transcranial Doppler sonography to test the CO_2 reactivity. No significant difference was found, also in patients with previous vasospasm.

The results are clinically not of primary importance, but the study is well done, the methodology used is correct and the results are adequately discussed.

R. Seiler

The authors report observations on the CO_2 reactivity of blood flow velocity in the middle cerebral arteries using transcranial Doppler ultrasound (TCD) in patients operated on for cerebral aneurysm.

The tests were performed at between 100 and 677 days after surgery. By this time 25 of 27 subarachnoid haemorrhage (SAH) patients had recovered to GOS 5. Exclusion criteria were major neurological or neuropsychological disability. Thus, the findings of no discernibly disturbed CO_2 reactivity in this subset are probably representative of the patient group having a very favourable outcome after SAH and clipping of the aneurysm. The same conclusion seems permissible with regard to patients having a good outcome after surgery for incidental aneurysm. It is nevertheless well known that brain infarction is not incompatible with a good outcome.

In 1989 a study on CO_2 reactivity was published showing decreasing CO_2 reactivity with increasing vasospasm after SAH [Hassler W, Chioffi F: CO_2 reactivity of cerebral vasospasm after aneurysmal subarachnoid haemorrhage. Acta Neurochir (Wien) 98: 167–175, 1989]. The study also briefly mentioned the normalisation of CO_2 reactivity when vasospasm had disappeared; however, no further data were given.

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