Three Cases of Hyperperfusion Syndrome Identified by Daily Transcranial Doppler Investigation After Carotid Surgery

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Background: cerebral hyperperfusion syndrome (HS), occurs in 0.5–1% of patients undergoing carotid endarterectomy (CEA), and may result in intracerebral haemorrhage and death. 

Aim: to diagnose HS by means of postoperative Transcranial Doppler (TCD).

Methods: between 1998 and 2001 nearly all 112 patients who underwent CEA were monitored for four days postoperatively by Transcranial Doppler.

Results: there were 3 patients with HS. All three showed TCD abnormalities hours before developing symptoms. One patient developed a full blown HS. Presumably, symptoms in the other two patients could be prevented by timely starting or restoring anti-hypertensive treatment.

Conclusion: daily TCD investigation in all patients undergoing CEA seems an effective strategy for the presymptomatic detection of HS.

Key Words: CEA; Hyperperfusion; Endarterectomy; Carotid artery; Carotid stenosis; Carotid surgery; Blood flow velocity; Ultrasonography; Hypertension; Transcranial Doppler; Cerebral arteries.

Introduction

The hyperperfusion syndrome (HS) is a rare but serious complication of carotid endarterectomy (CEA). Clinical signs include headache (often ipsilateral to the operated carotid artery), hypertension, seizures and focal neurological deficit. HS may result in brain oedema, intracerebral haemorrhage and ultimately death. The HS is thought to occur because of defective cerebral autoregulation in vessels accustomed to low perfusion pressures.\(^1\)\(^-\)\(^3\) It is accompanied by high flow velocities usually in the ipsilateral but occasionally in the contralateral intracranial vessels. High perfusion pressures at the level of the cerebral capillaries cause disruption of the blood brain barrier. Many investigators have noticed an interval of several days between surgery and the onset of HS.\(^2\)\(^-\)\(^7\) Symptoms may only occur after the patient has been discharged from hospital.

Most investigators agree that the HS is a potentially treatable condition.\(^3\)\(^-\)\(^8\) Adequate control of hypertension and even lowering of normal blood pressures are accepted interventions. Early recognition and treatment of HS is important to further minimise the perioperative risk of CEA.\(^9\)

We aimed to diagnose HS by routinely performing Transcranial Doppler (TCD) investigations during the first 4 days following CEA, based on the fact that HS is by definition accompanied by high intracranial flow velocities and based on the assumption that high flow velocities precede other symptoms of HS. This paper will describe our findings in three patients with signs of HS.

Methods

From July 1998 until January 2001 we studied 104/112 patients undergoing CEA by means of TCD shortly before surgery and for four days afterwards. Eight patients (7%) did not receive TCD because of an insufficient temporal window.

In general, only patients with a stenosis >70% (according to criteria of the European Carotid Surgery Trial\(^10\)\(^,\)\(^11\)) who had been symptomatic within the last 6 months were accepted for surgery. Patients with a recent stroke were not operated upon within 6 weeks.
of the incident. Surgery was performed under general anaesthesia with NO-inhalation and with the continuous infusion of remifentanil.

One patient died because of respiratory insufficiency due to an acute peritracheal haemorrhage. Another patient developed expansion of a pre-existing stroke due to HS. This paper describes the findings on TCD and arterial blood pressure (ABP) in this patient together with the findings in two other patients showing signs of HS who did not develop any serious complication.

TCD-measurements

We used Pioneer EME 2020 ultrasound equipment with a 2 MHz-pulsed Doppler transducer. The MCAs were insonated at depths varying from 45–66 mm (median 55 mm). Flow velocities were sampled at two or three depths at 2-mm intervals and the average was used for mean flow velocity (MFV) and of pulsatility index (PI). Investigations were performed 2 h before and 1–2 h after surgery as well as on the first 4 postoperative days. The same investigator performed all investigations in a single patient. Measurement depths were identical for each follow-up investigation.

Two SD intervals for normal changes after CEA of the MCA MFV and PI have been calculated at our institution from a series of nearly 100 uncomplicated procedures and served as reference for changes in individual patients.

Measurement of arterial blood pressure

All ABPs described in this paper were obtained from either hand-held or automatic manometric devices. 2 SD intervals for normal changes in systolic and diastolic ABP after CEA were calculated at our institution from a series of nearly 100 uncomplicated procedures and served as reference for changes in individual patients.

Case Descriptions

Case 1 – probable HS

A 54-year-old female with right-sided hypaesthesia of the cheek and neck region and an 85% stenosis of the left (35% right) internal carotid artery. Preoperative TCD suggested a right to left shunt via the anterior communicating artery. CT scan of the brain was normal. There were no changes in EEG during clamping, the patient did not require shunting and she awoke from anaesthesia without deficit. In the first postoperative hours periods of hypotension (100/35 mmHg) were treated with dopamine. During postoperative day 1 ABP's normalised and the patient could be transferred to the ward.

Follow-up TCD investigations (Fig. 1) at first seemed normal with a rise in MFV in both MCAs. However,
instead of returning to preoperative values on postoperative day 2 and 3 the MFV of the contralateral MCA went on to rise and reached values above the normal range on postoperative day 3. In addition, we observed a gradual but ongoing increase in both diastolic and systolic ABPs. These observations prompted us to designate the patient as probably suffering from HS. Though she had routinely been discharged from hospital on postoperative day 3, the vascular surgeon, at our advice, decided that she should return to hospital in order to receive anti-hypertensive treatment. She suffered a severe frontal headache. During oral treatment with enalapril on postoperative day 4 and onward her ABPs and the MFV of the contralateral MCA returned to normal levels. The headache subsided and further follow-up over a period of at least 3 months was uneventful.

Case 2 – definite HS

A 69-year-old female with hypertension previous right amaurosis fugax, severe bilateral carotid artery stenosis, and a left-sided hemiparesis. CT showed a watershed infarction in the right parieto–occipital region. TCD investigation showed neither extracranial to intracranial nor right to left shunting. The vertebral arteries, however, showed increased flow velocities (113 cm/s systolic). Right CEA was performed 10 weeks after stroke onset. During clamping EEG findings remained stable despite a drop in flow velocity over the ipsilateral MCA down to 40–50% of pre-clamp values. At clamp release a marked increase in MFV occurred over the ipsilateral MCA up to 138 cm/s (peak systolic 230 cm/s, not shown). Within a few minutes this high flow velocity normalised to a level only slightly higher than pre-clamp values. The patient awoke from surgery without neurological complaints.

During the first three postoperative days the patient was without complaints apart from a slight bifrontal headache. TCD measurements showed a temporary increase in MFV over the ipsilateral MCA with maximum on day 1 (mean 111 and peak systolic flow 208 cm/s). TCD measurements on day 3, however, showed a renewed increase instead of further decrease of ipsilateral MCA MFV accompanied by a gradual rise in ABP. It was decided that the patient should remain in hospital. On day 4 the patient developed a left sided focal status epilepticus. ABPs were up to 210/120 mmHg. TCD showed a further increase in flow velocity (mean 94 and peak systolic flow 127 cm/s, Fig. 2). The PI, which had shown a gradual rise during the first 3 postoperative days, showed a slight dip on postoperative day 4 and 5. The patient was transferred to the intensive care unit (ICU) and received intravenous clonazepam and valproate to control of her epilepsy as well as a continuous infusion with nitroprusside to keep systolic ABPs below 150 mmHg. Her status epilepticus subsided but a cortical myoclonus remained for days after the incident. EEG showed periodic lateralized epileptic discharges over the right motor cortex.

On postoperative days 4–6 a gradual normalisation of TCD findings paralleled clinical improvement. A CT scan 14 days after CEA showed a new lesion in the right frontal region as well as expansion of the previous watershed infarction. There was no haemorrhage or oedema.
velocities, far above the normal range. Though ABPs were normal we designated the patient as probably suffering a hyperperfusion syndrome and anti-hypertensive treatment was started immediately aiming to keep systolic ABPs below 150 mmHg. During the first postoperative day the patient required almost no hypertensive treatment. The ipsilateral MFV, however, remained far above the normal range and it was decided that the patient should remain in the ICU despite that he was without complaints.

On postoperative day 2 the ABP suddenly started to rise, reaching levels of 210/105 within a period of minutes. Treatment was started instantaneously: the patient received a continuous infusion with nitroglycerin. This caused the ABPs to return to normal levels. Over the postoperative days 1 to 4 we found a gradual rise in ipsilateral MCA PI. It was only when the PI reached levels of 1.2 and higher that the MFV started to return within normal limits. The patient could be transferred to the ward on postoperative day 4 and further follow up during at least 3 months was uneventful.

**Discussion**

In 1975 it was recognised that a minority of CEA patients developed a syndrome of increasing ABP, headache, seizures, focal neurological deficit, intracranial hemorrhage and, ultimately, death. SPECT studies demonstrated a marked increase in blood flow over the hemisphere on the side of surgery suggesting a loss of autoregulation. TCD studies showed very high blood flow velocities. The clinical findings together with ancillary investigations demonstrating increased blood flow or blood flow velocities have since been known as hyperperfusion syndrome (HS).

Several strategies have been advocated in order to select patients at risk for developing HS after CEA, either based upon pre-, per- or postoperative variables. Pre-operative variables, such as low pulsatility index, CT showed bilateral leucoaraiosis. On duplex there was a subtotal stenosis of the left and a 70% stenosis of the right carotid artery. During clamping at first a considerable asymmetry occurred in the patient’s EEG. However, by artificially increasing the patient’s ABP this asymmetry resolved and the endarterectomy could be performed without shunting. At clamp release, initially, high flow velocities were measured in the ipsilateral MCA (Fig. 3). These flow velocities normalized while the patient was still in the operation room and under general anaesthesia. However, after having regained consciousness and after having been transferred to the ICU we found very high MCA flow velocities, far above the normal range. Though ABPs were normal we designated the patient as probably suffering a hyperperfusion syndrome and anti-hypertensive treatment was started immediately aiming to keep systolic ABPs below 150 mmHg. During the first postoperative day the patient required almost no hypertensive treatment. The ipsilateral MFV, however, remained far above the normal range and it was decided that the patient should remain in the ICU despite that he was without complaints.

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**Case 3 – definite HS**

A 79-year-old male patient with left amaurosis fugax, and multiple right transient ischaemic attacks (TIAs). CT showed bilateral leucoaraiosis. On duplex there was a subtotal stenosis of the left and a 70% stenosis of the right carotid artery. During clamping at first a considerable asymmetry occurred in the patient’s EEG. However, by artificially increasing the patient’s ABP this asymmetry resolved and the endarterectomy could be performed without shunting. At clamp release, initially, high flow velocities were measured in the ipsilateral MCA (Fig. 3). These flow velocities normalized while the patient was still in the operation room and under general anaesthesia. However, after having regained consciousness and after having been transferred to the ICU we found very high MCA flow velocities, far above the normal range. Though ABPs were normal we designated the patient as probably suffering a hyperperfusion syndrome and anti-hypertensive treatment was started immediately aiming to keep systolic ABPs below 150 mmHg. During the first postoperative day the patient required almost no hypertensive treatment. The ipsilateral MFV, however, remained far above the normal range and it was decided that the patient should remain in the ICU despite that he was without complaints.

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velocities in ipsi- (or contralateral) MCA together with (2) (surges of) hypertension. Velocities should be at least doubled with respect to preoperative measurements. They should occur either prior to or after postoperative day 1 since, in our experience, increases of mean MCA flow velocity up to 210% of preoperative values on postoperative day 1 may occur normally. ABPs should reach levels comparable to that of malignant hypertension (systolic ABP at 200 mmHg or above and diastolic ABP at 100 mmHg or above). Headache, as often mentioned third symptom of HS, is not a very sensitive sign either, given our case 3 who remained without complaints despite the combination of markedly elevated MCA flow velocities and ABPs up 210/105.

Of course, the occurrence of focal epileptic seizures, focal neurological deficit, intracranial haemorrhage and/or intracranial oedema in addition to the increased intracranial flow velocities will provide certainty to the diagnosis HS. These symptoms, however, should not be considered obligatory for the diagnosis. One cannot postpone therapeutic measures until the stage that these symptoms develop.

In cases 2 and 3 the high MCA flow velocities were observed hours to almost a day prior to other signs of HS, especially prior to an abnormal increase in ABP. Thus, TCD seems a more valuable tool for the presymptomatic diagnosis of HS than the monitoring of ABP alone. Furthermore, Figures 2 and 3 illustrate how difficult it is to determine the onset of HS on basis of ABP: measurements of ABP are highly variable, even on an ICU where patients are supine and at rest. Finally, as observed in case 3, rises in ABP due to HS may develop within minutes and can easily be missed when ABPs are measured on, for instance, an hourly basis. Monitoring patients after CEA by means of daily TCD seems to provide more consistent data and, thereby, allows more confident clinical decision making than monitoring patients by measuring ABP alone.

Based upon these findings we developed the following strategy. Any patient developing abnormally high MCA flow velocities during the first few days after CEA deserves the diagnosis “probable HS”, especially when high flow velocities occur before or after postoperative day 1. Such a patient should be transferred to the ICU for monitoring of ABP. Antihypertensive treatment should aim to keep systolic ABPs below 150 mmHg and diastolic ABPs below 90 mmHg. Ideally, the patient will never develop hypertensive surges and, consequently, never reach the diagnosis “definite HS”. The end of the patient’s critical period will be announced by a gradual return of MCA flow velocity within normal limits. The patient can be discharged from the ICU. Future research will have to establish the effectiveness of this strategy.

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Detailed data on normal values for mean and peak flow velocities and pulsatility index as well as arterial blood pressures can be obtained from the corresponding author on demand.

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