European Review for Medical and Pharmacological Sciences 2014; 18: 1176-1180

Neurological symptoms associated with cerebral hyperperfusion syndrome after CEA and CAS – one centre study

D. ZIAJA, G. BIOLIK, P. KOCEŁAK[1], M. SZNAPKA, P. JANAS[2], A. CZAJKA, J. CHUDEK[1], K. ZIAJA

Department of General and Vascular Surgery, Medical University of Silesia Katowice, Poland
[1]Department of Pathophysiology, Medical University of Silesia Katowice, Katowice, Poland
[2]Neurological Outpatient Clinic, Upper-Silesian Medical Centre, Katowice, Poland

Abstract. – BACKGROUND: There are two equivalent in efficacy methods of the treatment of carotid artery stenosis: endarterectomy (CEA) and stenting (CAS), in which the blood flow increases in most patients by 20-40% over baseline, in some exceeding 100% and being symptomatic and leading to cerebral hyperperfusion syndrome (CHS).

AIM: The aim of this study is to analyze the structure of neurological symptoms associated with CHS in patients with carotid artery revascularization.

PATIENTS AND METHODS: Retrospective analysis included 1386 consecutive patients treated in the Department of General and Vascular Surgery between 2005 and 2011, with 625 of them were subjected to CEA and 761 to CAS. If neurological symptoms occurred, patients were consulted by a neurologist and ultrasonography (USG) examination and CT were performed. Neurological symptoms in patients with new onset of headache ipsilateral to the carotid revascularization were extracted from medical records and nursing documentation.

RESULTS: Neurological symptoms attributed to CHS were observed in 66 (10.6%) of CEA and 61 (8.0 %) of CAS group. The frequency was similar in both groups (p = 0.43). The occurrence of epileptic attacks was similar in both study groups. The only difference was the less frequent falling of the lip in CAS group. Transient bradycardia and/or hypotension were observed in CAS (8.8% vs. 10.4% and 1.3% vs. 1.3%, respectively). No difference in stroke appearance between groups were found.

CONCLUSIONS: The occurrence of neurological symptoms attributable to cerebral hyperperfusion syndrome after carotid artery revascularization in short term observation is similar regardless of the method used.

Key words:
Cerebral hyperperfusion syndrome (CHS), Carotid artery revascularization, Carotid endarterectomy (CEA), Carotid artery stenting (CAS).

Introduction

There are two equivalent in efficacy methods of the treatment of carotid artery stenosis: endarterectomy (CEA – carotid endarterectomy)[1,2] and stenting (CAS – carotid stenting)[3,4]. After carotid revascularization the blood flow increases in most patients by 20-40% over baseline, lasting for several hours[5]. In some, hyperaemia occurs with an increase of cerebral blood flow to levels of 100-200% over baseline[4] and falls to a steady state by several postoperative days but can last up to 2 weeks[6]. Intracranial vascular bed hyperperfusion (> 100% increase over baseline), especially in vertebrobasilar circulation[7] occurs in a subset of these patients and a few of them become symptomatic[6].

Both procedures may cause cerebral hyperperfusion syndrome (CHS)[8,9] defined as increase in cerebral blood flow (CBF) over 100% compared to baseline with new onset of headache ipsilateral to the carotid revascularization with or without focal neurological deficits and seizures[10] (eye and face pain, vomiting, confusion, visual disturbances, focal neurological deficits, focal motor seizures and intracerebral or subarachnoid haemorrhage)[5]. Most studies report up to 3% prevalence[11,12]. Potential risk factors for the development of CHS include comorbidity (i.e. diabetes mellitus, hypertension, patients before CABG (coronary artery bypass graft) with low ejection fraction (EF) and medication, and flow-related factors associated with operative technique. It seems that factors like diminished cerebrovascular reserve, postoperative hypertension, and hyperperfusion that lasts more than several hours[5] play a crucial role. It is thought that CHS results from loss of vascular autoregulatory mechanisms in chronically hypoperfused hemisphere[8].

Corresponding Author: Jerzy Chudek, MD, Ph.D; e-mail: chj@poczta.fm

However, the symptoms of CHS are non-specific and may be treated as the symptoms of other post-operative complications (neurogical deficit after stroke, hypotension)[5].

The aim of this study is to analyze the structure of neurological symptoms attributable to CHS in patients with carotid artery stenosis treated by carotid endarterectomy and percutaneous carotid angioplasty.

Patients and Methods

Retrospective analysis included 1386 consecutive patients treated for stenosis within extracranial segment of internal carotid artery in the Department of General and Vascular Surgery of Medical University of Silesia in Katowice between 2005 and 2011, with 625 of them were subjected to carotid endarterectomy (CEA) and 761 to percutaneous carotid angioplasty and stenting (CAS).

321 (23.1%) patients (176 before CEA, 145 before CAS) reported past stroke and/or transient ischaemic attack (TIA), in 234 neurological deficits were observed and were not evaluated by the neurologist before revascularization procedure as neurological tests were not performed routinely before revascularisation procedure.

In all the patients the grade of the carotid artery stenosis was verified by duplex-ultrasound according to NASCET (The North American Symptomatic Carotid Endarterectomy Trial) criteria. Qualification of the patients for reconstructive procedure was the degree of stenosis > 60% qualified patients for CABG and > 70% in the patients with neurological complaints. The choice of the procedure was based on the analysis of plaque intra-luminal surface (Rutherford classification)[13] and grey-scale median score (GSM) echogenicity score[14]. Those with a score below 25, typical for unstable plaque, were referred to the eversion method of CEA, while the others to CAS.

Reconstructive procedure

All the patients qualified for CAS received acetylsalicylic acid (150 mg daily) and clopidogrel (75 mg daily) for at least two days before the procedure. Eversion CEA was performed in local anesthesia with maintained verbal contact during the procedure. Before probationary clamping of common carotid artery 5,000 units of unfractionated heparin (UFH) was given intravenously. Only in 3 patients the necessity of shunt during the procedure occurred.

CAS procedures were performed with neuroprotection preferentially by the right femoral artery in radiology operating theater. Each patient received intravenously 2500 units of UFH after cannulation of femoral artery and 0.5-1.0 mg of atropine directly before stent implantation. All endovascular procedures were performed with distal neuroprotection.

Data collection

Restrictive post-procedure observation was carried out in intensive care unit (ICU) during first 24 to 48 hours after revascularization, initially by anesthesiologist (first 2 h), then by a physician, neurologist and experienced nurse team at conditions of increased postoperative surveillance. Patients remained under the supervision of a cardiologist and a neurologist, and qualified team of nurses. If neurological symptoms occurred, each patient was consulted by a neurologist and USG examination (to exclude thrombosis) and CT were performed to exclude ischemic and/or hemorrhagic stroke. The CT imaging was repeated after 24 h.

Neurological sign and symptoms were extracted from medical records and nursing documentation. Those not related to ischemic stroke were attributed to hyperperfusion syndrome (CHS) when occurred in a patient with new onset of headache ipsilateral to the carotid revascularization.

Statistical analysis

Statistical analysis was performed using the software package Statistica 8.0 PL (StatSoft Inc., Tulsa, OK, USA). Results are presented as mean values or percentages for CEA and CAS groups, separately. Chi^2 and *t*-test were applied. The value of $p < 0.05$ is deemed as statistically significant.

Results

Study group characteristics

Patients qualified for CAS were slightly older and had significantly tighter carotid artery stenosis in average. The prevalence of hypertension, chronic kidney disease, peripheral arterial disease, past stroke episodes was greater, but the percentage of past myocardial infarcts and coronary revascularisation procedures was smaller in CEA than CAS group (Table I).

Table I. Characteristics of study groups (n=1386).

	CEA (N=625)	CAS (N=761)	Statistical significance
Age [years]	70 (57-82)	73 (62-83)	Ns
Carotid artery stenosis [%]	80 (76-84)	86 (81-91)	<0.001
Concomitant diseases [n (%)]			
Prior stroke or TIA	176 (28.1)	145 (19.0)	<0.001
Coronary artery disease	375 (60.0)	449 (59.0)	Ns
Past myocardial infarction	124 (19.8)	94 (12.3)	<0.001
Past PCI or CABG	93 (14.8)	158 (20.4)	0.006
Peripheral arterial disease	137 (21.9)	59 (7.7)	<0.001
Arterial hypertension	489 (78.2)	395 (51.9)	<0.001
Diabetes mellitus	70 (11.2)	123 (16.1)	0.01
Chronic kidney disease*	68 (11.0)	57 (7.4)	0.04

*defined as serum creatinine concentration > 1.5 mg/dl
PCI – percutaneous coronary intervention
CABG – coronary artery bypass graft
Ns – not significant

Neurological symptoms associated with CHS

Neurological symptoms attributed to CHS was observed in 66 (10.6%) of CEA and 61 (8.0%) of CAS group. The frequency was similar in both groups ($p = 0.43$).

The most common neurological symptom that was observed between 2 and 12 hour after procedure (in the first two hours patients were under anaesthesiologist team control) was the numbness of the opposite limb. The symptom was reported with similar frequency in both groups (9.6% after CEA and 7.1% after CAS). A weakening of the muscle strength of the opposite limbs was also frequently stated with equal frequency in both groups.

Epileptic attacks were reported in 21 patients with similar frequency in both study groups. The only difference was the less frequent falling of the lips in CAS group (Table II).

Symptoms attributed to sympathetic nervous system dysregulation

Both episodes of transient bradycardia and/or hypotension were observed with similar frequency between CAS and CEA group (8.8% vs. 10.4% and 1.3% vs. 1.3%, respectively).

Stroke and fatal outcome

Neurological deficit with documented stroke in CT was observed in 22 patients (3.5%) after CEA and in 18 patients (2.4%) after CAS up to the 30th day post procedure. More than half strokes had ischemic etiology (13 and 8, respectively). In one third of the patients with stroke (N=14) symptoms of hemiparesis subsided without permanent neurological deficit.

During the first 30 days 10 patients died (1.6%) in CEA group and 6 patients (0.8%) in CAS group. All death episodes were in patients with previous cardiovascular co-morbidities (stroke, myocardial infarction, abdominal aorta aneurysm, peripheral artery disease in the last 6 months).

Table II. Neurological symptoms observed within the first 48 hours post-procedure.

	CEA (N=625)	CAS (N=761)	Statistical significance
Numbness of the opposite limb (paresthesia)	60 (9.6%)	54 (7.1%)	Ns
Buccal trembling (habit chorea)	8 (1.3%)	13 (1.7%)	Ns
Falling of the lip	31 (5.0%)	4 (0.5%)	<0.001
Weakening of the muscle strength within the upper limb on the opposite side	39 (6.2%)	46 (6.0%)	Ns
Weakening of the muscle strength within the lower limb on the opposite side	29 (4.6%)	49 (6.4%)	Ns
Seizures	7 (1.1%)	14 (1.8%)	Ns

CEA – carotid artery endarterectomy
CAS – carotid artery stenting
Ns – not significant

Discussion

The study reports similar frequency of neurological symptoms (focal deficits and seizures) attributed to CHS that occurred during first 12 hours after revascularization procedure, regardless of the method of carotid revascularization used. Our results suggest that the occurrence of CHS with neurological symptoms after CEA and CAS is comparable, as previously shown by Ogasawara et al[15], and in line with similar spectrum of risk factors for CHS in both groups[16]. Additionally, some previous studies reported that clinical manifestation of CHS after both procedures is the same, but the prognosis and outcomes differ and seem to be worse after CAS than after CEA[17,18]. Moreover, other studies showed that the course of CHS after these procedures vary, as CHS usually occurs 5 to 7 days after CEA[15], and within the first 24 hours after CAS[15,17,19]. Our data demonstrate that neurological symptoms attributable to CHS develop equally frequently after CEA and CAS within the first 12 hours post procedure. Coutts et al.[17] differentiated CHS into three types: two occurring within hours after carotid interventions due to acute focal edema and acute hemorrhage, and classic delayed type occurring at least 24 hours after procedure, with different association with intracranial hemorrhage and mortality[17].

So far reported prevalence of CHS in patients after carotid endarterectomy differs in a wide range from 0.2 to 18.9%. The differences result from criteria CHS applied. Most of studies report the development of CHS in subjects with the evidence of hyperperfusion increase of more than 100% from baseline[12,16,20,21]. These studies excluded neurological symptoms that were developed without confirmed hyperperfusion. This more restrictive definition diminishes the appearance of neurological symptoms potentially attributable to CHS[22].

In one single-center study a prevalence of CHS after CEA was estimated at 1.45% and its diagnosis was based on the occurrence of neurological symptoms with the exclusion of stroke or transient ischemic attack made by a neurologist and the evidence of sulcal effacement in CT scan and the prevalence of CHS was comparable to those of TIA and cerebrovascular accidents which suggests[16] that neurological symptoms after carotid artery revascularization are more common than the prevalence of CHS.

One of the studies proposes the algorithm for work-up of patients with symptoms suggestive of CHS after CEA with the use of echo duplex carotid artery, first procedure for exclusion of occlusion or thrombosis of carotid artery as a postoperative complication, and, then, computed tomography for visualization of new abnormalities and alternative diagnosis in the case of no occlusion of artery. Transcranial Doppler is recommended for the evaluation of cerebral perfusion if no new brain abnormalities are detected and, then, lack of alleviation of symptoms after initiation of normalization of cerebral blood flow enables a CHS diagnosis[23].

Headache is commonly reported after CEA (in 62% procedures) and is one of the symptoms of CHS, but in CHS it is more intense and pounding[24]. Our analysis was focused on focal deficits and seizures in patients with new onset of headache ipsilateral to the carotid revascularization after exclusion of ischemic stroke. The frequency of analyzed symptoms after CEA and CAS was similar with the exception of the incidents of unilateral falling of the lips. It may be the result of the irritation of branches in the ramus mandibularis of the facial nerve during the procedure not related to CHS.

In addition to symptoms of CHS we analyzed the prevalence of episodes of transient bradycardia and/or hypotension. Both episodes were more frequently observed in CAS than in CEA group (8.8% vs. 10.4% and 1.3% vs. 1.3%, respectively). It seems that these complications are the results of a catheter instrumentation of the carotid bulb[25] which stimulates carotid baroreceptors. The baroreceptors stimulation may represents as hemodynamic depression[26] with bradycardia related to parasympathetic discharge and hypotension due to inhibition of the sympathetic tone[26]. Therefore, these symptoms are not related to CHS but co-occurred with CHS.

We did not control the hemodynamic changes post procedure routinely and, thus, we could not determine which symptoms occurred were accompanied by at least doubling in cerebral blood flow in patients with new onset of headache ipsilateral to the carotid revascularization. We perform duplex Doppler sonography only for internal carotid artery (ICA) patency checking. This study had a retrospective design that enabled the precise analysis of the time of symptom occurrence, and longer than 12 hours analysis. The analysis of symptoms of reperfusion syndrome was difficult in the group of patients with a history of stroke and neurological deficits. Moreover, distinguishing symptoms caused by post procedure hyperperfusion and microembolism has not been possible.

Conclusions

The occurrence of neurological symptoms attributable to cerebral hyperperfusion syndrome after carotid artery revascularization in short term observation is similar regardless of the method used.

Conflict of interest

None of the Authors declares conflict of interest

References

1) Chambers BR, Donnan GA. Carotid endarterectomy for asymptomatic carotid stenosis. Cochrane Database of Syst Rev 2005; (4): CD001923.
2) Cina CS, Clase CM, Haynes RB. Carotid endarterectomy for symptomatic carotid stenosis. Cochrane Database Syst Rev 2000; (2): CD001081.
3) CAVATAS Investigators. Endovascular versus surgical treatment in patients with carotid stenosis in the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS): a randomized trial. Lancet 2001; 357: 1729-1737.
4) Yadav JS, Wholey MH, Kuntz RE, Fayad P, Katzen BT, Mishkel GJ, Bajwa TK, Whitlow P, Strickman NE, Jaff MR, Popma JJ, Snead DB, Cutlip DE, Firth BG, Ouriel K. Protected carotid-artery stenting versus endarterectomy in high-risk patients. N Engl J Med 2004; 351: 1493-1501.
5) Naylor AR, Evans J, Thompson MM, London NJ, Abbott RJ, Cherryman G, Bell PR. Seizures after carotid endarterectomy: hyperperfusion, dysautoregulation or hypertensive encephalopathy? Eur J Vasc Endovasc Surg 2003; 26: 39-44.
6) Jørgensen LG, Schroeder TV. Defective cerebrovascular autoregulation after carotid endarterectomy. Eur J Vasc Surg 1993; 7: 370-379.
7) Schwartz RB. Hyperperfusion encephalopathies: hypertensive encephalopathy and related conditions. Neurologist 2002; 8: 22-34.
8) Sundt TM Jr, Sharbrough FW, Piepgras DG, Kearns TP, Messick JM Jr, O'Fallon WM. Correlation of cerebral blood flow and electroencephalographic changes during carotid endarterectomy: with results of surgery and hemodynamics of cerebral ischemia. Mayo Clin Proc 1981; 56: 533-543.
9) McCabe DJ, Brown MM, Clifton A. Fatal cerebral reperfusion hemorrhage after carotid stenting. Stroke 1999; 30: 2483-2486.
10) Wu T, Anderson N, Barber P. Neurological complications of carotid revascularization. J Neurol Neurosurg Psychiatry 2012; 83: 543-550.
11) Dunne VG, Besser M, Ma WJ. Transcranial Doppler in carotid endarterectomy. J Clin Neurosci 2001; 8: 140-145.
12) Beard JD, Mountney J, Wilkinson JM, Payne A, Dicks J, Mitton D. Prevention of postoperative wound haematomas and hyperperfusion following carotid endarterectomy. Eur J Vasc Endovasc Surg 2001; 21: 490-493.
13) Rutherford RB, Baker JD, Ernst C, Johnston KW, Porter JM, Ahn S, Jones DN. Recommended standards for reports dealing with lower extremity ischemia: revised version. J Vasc Surg 1997; 26: 517-538.
14) Denzel C, Balzer K, Muller KM, Fellner F, Fellner C, Lang W. Relative value of normalized sonographic in vitro analysis of arteriosclerotic plaques of internal carotid artery. Stroke 2003; 34: 1901e6.
15) Ogasawara K, Sakai N, Kuroiwa T, Hosoda K, Iihara K, Toyoda K, Sakai C, Nagata I, Ogawa A. Intracranial hemorrhage associated with cerebral hyperperfusion syndrome following carotid endarterectomy and carotid artery stenting: retrospective review of 4494 patients. J Neurosurg 2007; 107: 1130-1136.
16) Brantley H, Kiessling J, Milteer H, Mendelson F. Hyperperfusion syndrome following carotid artery stenting: the largest single-operator series to date. J Invasive Cardiol 2009; 21: 27-30.
17) Coutts SB, Hill MD, Hu WY. Hyperperfusion syndrome: toward a stricter definition. Neurosurgery 2003; 53: 1053-1060.
18) Meyers PM, Higashida RT, Phatouros CC, Malek AM, Lempert TE, Dowd CF, Halbach VV. Cerebral hyperperfusion syndrome after percutaneous transluminal stenting of the craniocervical arteries. Neurosurgery 2000; 47: 335-343.
19) Abou-Chebl A, Yadav JS, Reginelli JP, Bajzer C, Bhatt D, Krieger DW. Intracranial hemorrhage and hyperperfusion syndrome following carotid artery stenting: risk factors, prevention, and treatment. J Am Coll Cardiol 2004; 43: 1596-1601.
20) Shields RC. Medical management of carotid stenosis. Perspect Vasc Surg Endovasc Ther 2010; 22: 18-27.
21) Yoshimoto T, Shirasaka T, Yoshizumi T, Fujimoto S, Kaneko S, Kashiwaba T. Evaluation of carotid distal pressure for prevention of hyperperfusion after carotid endarterectomy. Surg Neurol 2005; 63: 554-557.
22) Karapanayiotides T, Meuli R, Devuyst G, Piechowski-Jozwiak B, Dawarrrat A, Ruchat P, Von Seqesser L, Bogousslavsky J. Postcarotid endarterectomy hyperperfusion or reperfusion syndrome. Stroke 2005; 36: 21-26.
23) van Mook W, Rennenberg R, Schurink G, van Oostenbrugge RJ, Mess WH, Hofman PA, de Leeuw PW. Cerebral hyperperfusion syndrome. Lancet Neurol 2005; 4: 877-888.
24) Tehindrazanarivelo AD, Lutz G, PetitJean C, Bousser MG. Headache following carotid endarterectomy: a prospective study. Cephalalgia 1992; 12: 380-382.
25) Qureshi AI, Luft AR, Sharma M, Janardhan V, Lopes DK, Khan J, Guterman LR, Hopkins LN. Frequency and determinants of postprocedural hemodynamic instability after carotid angioplasty and stenting. Stroke 1999; 30: 2086-2093.
26) Harrop JS, Sharan AD, Benitez RP, Armonda R, Thomas J, Rosenwasser RH. Prevention of carotid angioplasty-induced bradycardia and hypotension with temporary venous pacemakers. Neurosurgery 2001; 49: 814-820.