Brain Disorders & Therapy

Litovchenko and Iakubenko, Brain Disord Ther
2015, 4:2
http://dx.doi.org/10.4172/2168-975X.1000161

Research Article Open Access

Identification of Disturbances of Autoregulation of Cerebral Hemodynamics and Blood Vessels Reactivity in Patients with Consequences of Mild Traumatic Brain Injuries

Litovchenko T and Iakubenko I*

Department of Neurology, Kharkiv Medical Academy of Postgraduate Education, Kharkiv, Ukraine

***Corresponding author:** Iakubenko I, Department of Neurology, Kharkiv Medical Academy of Postgraduate Education, Kharkiv, Ukraine, Tel: +39 3384992107; E-mail: yakubenko.yulya@mail.ru

Rec date: Jan 6, 2015, **Acc date:** Jan 30, 2015, **Pub date:** Feb 7, 2015

Abstract

The purpose of the current research was to revise the disturbances of autoregulation of cerebral hemodynamics and reactivity of vessels in patients with consequences of mild traumatic brain injuries by using Doppler ultrasonography with hyper-and hypocapnic tests.

Methods: We examined 65 patients with consequences of mild traumatic brain injuries. Doppler ultrasonography with hyper-and hypocapnic tests were carried out according to the standard method.

Results: During the research by Doppler ultrasonography with the hypercapnic and hypocapnic tests in patients with consequences of mild TBI the coefficient of overshoot of 1.13 ± 0.04 was identified. A paradoxical cerebral vascular response was evident as a delayed response to the tests as carried out. The above response was accompanied by the increase of the LVF after the hypercapnic test to 28.7% (48.8% in the control group) and by the increase of the LVF after the hypocapnic test to 36.8% (27.5% in the control group). Under the hypercapnic load in patients with consequences of mild TBI the coefficient of reactivity was lower than that of the patients in the control group (0.34 ± 0.07 and 0.46 ± 0.03 RVU respectively, $p<0.05$). Under the hypocapnic load in patients with consequences of mild TBI the coefficient of reactivity was lower than that of healthy subjects (0.44 ± 0.02 and 0.55 ± 0.04 RVU respectively, $p<0.05$). The index of vasomotor reactivity in patients with TBI consequences was lower, than that of the control group (73.1 ± 0.05 and 97.3 ± 0.02 respectively, $p<0.0001$). The increase of PI up to 1.73 ± 0.02; and the increase of RI up to 0.97 ± 0.02 ($p<0.0001$) were present in all the patients in the survey sample with consequences of traumatic brain injuries.

Conclusions: During our investigation we detected changes of reactivity of vessels towards the decrease of indicators of linear velocity of blood flow under the tests. A paradoxical vascular response was marked in all the patients under the hyper- and hypocapnic load; a test-induced delayed vessels reaction was marked in 52 out of 65 patients.

Keywords: Traumatic brain injury; Consequences of mild traumatic brain injury; Cerebral autoregulation, Reactivity of vessels

Introduction

Traumatic brain injury (TBI) is frequently referred to as the silent epidemic because the problems that result from it (e.g., impaired memory) often are not visible. Mild traumatic brain injury (MTBI) accounts for at least 75 percent of all traumatic brain injuries in the United States. However, it is clear that the consequences of MTBI are often not mild [1-4].

TBI-induced pathogenesis is multifocal and includes various pathophysiological and pathobiochemical processes: oxidative stress, excitotoxicity, perifocal neuron depolarization (within the first minutes & hours after the trauma), autoimmune inflammation, apoptosis (within further days & weeks) etc. In the long run all these mechanisms lead to the loss of neurons and neural bonds between different parts of CNS [5-8].

In a long-term perspective TBI generates 'posttraumatic syndrome', marked by a headache, dizziness, tiredness, low mood and memory impairment. Depending on its severity and type, TBI results in primary structural-functional brain damage differing in abundance and degree at the subcellular, cellular, tissular and organ level; besides, central regulation of vital functions may be disturbed. Mild traumatic brain injury is a mild case of a diffuse axonal injury. It is recognized that clinical aspects of mild traumatic brain injury are conditioned by asynapsia, mainly functional, between the cerebral cortex, subcortical structures and brain stem. Morphologic substrate of mild traumatic brain injury includes synaptic apparatus and redistribution of interstitial fluid. Disturbed circulation may also be registered in case of mild traumatic brain injury, arising from small vessels lesions and white matter capillaropathy [4,5,9].

The involving of brain stems structures provokes both specific and nonspecific brain systems impairment, manifesting as autonomic and neuropsychological disorders. Mild TBI-induced lesion of limbic-reticular complex leads to circulatory disturbance and to cerebral synaptic apparatus disorder. In the following reticulo-cortico-

subcortical malfunction is complicated by dyscirculatory alterations, neurohumoral, neurohormonal and metabolic derangements, produced by a 'tension mechanism', common to a stressful situation [7,8,10-12].

Mild TBI primary structural changes trigger the initiation of neurometabolic pathway, generally at ultrastructural level. These alterations factor into tissue hypoxia progression and acid intoxication. Brain injury originates cerebral autoregulation disorder, liquor-dynamic disturbances and alterations in hematoencephalic barrier permeability. Cerebral autoregulation is one of the *fundamental properties* of the *cerebral circulation*. It is of fundamental importance for adequate cerebral blood supply and it is defined by cerebral vessels' capacity to hold constant volume velocity of cerebral blood flow on a change of perfusion pressure. Changes in cerebral vessels reactivity may represent a diagnostic character, as well as they may describe cerebral circulation functional status [13-15].

The purpose of the current research was to revise the disturbances of autoregulation of cerebral hemodynamics and reactivity of vessels in patients with consequences of mild traumatic brain injuries (TBI) by using Doppler ultrasonography with hyper-and hypocapnic tests.

Materials and Methods

We examined 65 patients with consequences of mild traumatic brain injuries, at the age of 25- 35, where 50 male and 15 female patients. The duration of the disease was 2-3 years. All the patients were subject to comprehensive clinical neurological exam. Basic syndromes detected in patients were: cephalalgias, asthenic syndrome and dysautonomia, that is consistent with literature data [5,9,13]. All the patients present the following problems: headaches (98.7%), rapid fatigability (82.2%), attention and memory impairment (32.8%), dizziness (10.6%), acrimony (52.4%), anxiety (47.8%), sleep problems (27.4%). In neurologic status symptomatology was observed in the form of decrease of convergence (68.2%), asymmetry of face (76.8%), revivals of tendinous reflexes (78.5%), asymmetry of tendinous reflexes (63.6%), paleness of skin cover (37.7%), red *dermographism* (78.3%), white *dermographism* (27.7%).

The examination did not cover patients with a concurrent actual somatic pathology.

The control group included 30 apparently healthy subjects (20 men and 10 women), gender and age-coinciding with the survey sample.

To evaluate hemodynamic index of linear velocity of blood flow (LVF) and indicators of reactivity of vessels in the system of the common carotid arteries (common, external and internal carotid arteries), all the patients were examined by the method of Doppler ultrasonography (the supersonic apparatus E SAOTE Megas GPX 2004, the linear detector 7.5-10 MHz). The assessment was performed by standardized method. To determine cerebral vessels reactivity hypercapnic and hypocapnic tests were applied. Hypercapnic test was exercised by a post- inhalation breath-holding up to 30 sec. with a cerebral blood flow measurement immediately prior to exhalation. Hypocapnic test was exercised after the hypercapnic one, by way of frequent and deep breathing during 30 sec. None of the patients showed clear signs of distress due to the tests. Before conducting the compression tests, routine Doppler ultrasonography of vessels of common, external and internal carotid arteries was carried in all the patients in order to exclude coiling, occlusion and hemodynamically relevant stenosis.

In our study, in order to estimate hemodynamics and reactivity of vessels in the carotid arterial system, we took into consideration the primary average LVF (aLVF), systolic linear velocity of blood flow (sLVF), the pulsation index (PI) and the index of peripheral resistance (RI). We estimated V0-the average LVF at a baseline, V1-the average LVF during the hypercapnia, V2-the average LVF during the hypocapnia, overshoot (vicarious increase of LVF in response to hypercapnia).

We calculated the coefficient of overshoot (CO), the coefficient of reactivity during the hypercapnia (CR+), the coefficient of reactivity during the hypocapnia (CR-), the index of vasomotor reactivity (IVMR).

The coefficient of overshoot (CO) was calculated by the formula [13-16]:

$$CO = V1 / V0,$$

in which V0 means the average LVF at a baseline,

V1 means the average LVF during the hypercapnia.

The coefficient of reactivity during the hypercapnia (CR+) was calculated by the formula [13,16,17]:

$$CR+ = (V1/V0)-1$$

in which V0 means the average LVF at a baseline,

V1 means the average LVF during the hypercapnia.

The coefficient of reactivity during the hypocapnia (CR-) was calculated by the formula [13,16,17]:

$$CR- = 1-(V2/V0)$$

in which V0 means the average LVF at a baseline,

V2 means the average LVF during the hypocapnia.

The index of vasomotor reactivity (IVMR) was calculated by the formula [13,16,17]:

$$IVMR = ((V1-V2)/V0) *100\%$$

in which V0 means the average LVF at a baseline,

V1 means the average LVF during the hypercapnia,

V2 means the average LVF during the hypocapnia.

The data received were mathematically processed by analysis-of-variance method (Student's t-test and Fischer test); correlation relationship was estimated using program packages Excel XP build 10.6612.6625-SP3 (Microsoft), Statistica 6.0 (Statsoft Inc)

Results and Discussion

Spectrographic shapes of the arterial system in question significantly differ. Analysis of Doppler-shifted spectrum allows classifying them as arteries with a low, mean and high peripheral vascular resistance (PVR). PVR level depends on the region, wherein a targeted artery supplies blood. Thus, the blood flow in the internal carotid artery, ensuring direct cerebral tissues perfusion, has a low peripheral resistance. In the external carotid artery, ensuring principally soft head tissues perfusion, the blood flow is described by a high peripheral resistance. The blood flow in the common carotid artery is characterized by a mean peripheral resistance. The PVR value models dopplerogram, sizes up magnitudes of telediastolic flow

velocity and determines the nature of the audible signal. In this regard, it is in internal carotid arteries that hemodynamic parameter is appropriate to evaluate [2,16,17].

In estimating dopplerographic curves for arteries with a low peripheral vascular resistance the following peaks can be distinguished on a pulsed wave curve: 1-systolic peak: corresponds to a blood peak flow within the ejection period; 2-catacrotic wave: corresponds to the entry in the period of relaxation; 3-dicrotic wave: characterizes the closing period of the aortic valve; 4-diastolic phase: corresponds to ventricular diastole phase [13,16-18].

Patients with consequences of traumatic brain injuries demonstrated paradoxical (abnormal) vascular response that can be represented in 2 types:

- type 1-increase of peak systolic velocity of blood flow up to 12% on the average in the internal carotid artery in response to hypercapnia, with no decrease of blood flow velocity in the next phase of hypocapnia, with a parallel decrease of peripheral resistance index (RI) (Figure 1).

- type 2-paradoxical vascular response to hypercapnia in terms of decrease of velocity or its delayed increase with a further velocity gain in response to hypocapnia with a parallel increase of peripheral resistance index (RI), presumably related to a malfunction of vasomotor mechanisms of peripheral minute vessels (Figure 2).

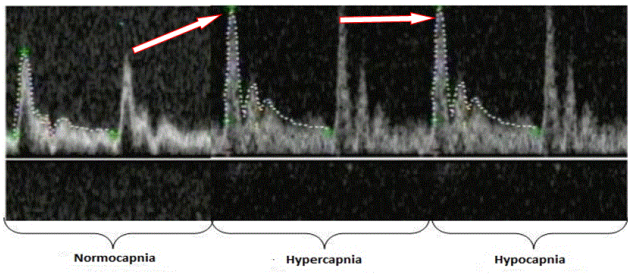

Figure 1: Variant of cerebral vessels reactivity malfunction in patients with consequences of traumatic brain injuries (type 1).

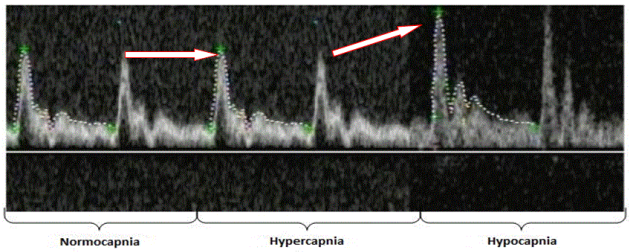

Figure 2: Variant of cerebral vessels reactivity malfunction in patients with consequences of traumatic brain injuries (type 2).

After the hypercapnia a transient increase of the blood flow owing to the compensatory vasodilatation was registered in the patients of the control group. The above can be used as an indicator of autoregulation. Temporary hyperemic response in carotid system vessels, manifesting as a short-term LVF increase, allows calculating the index, characterizing the vasodilatation in response to a transient decrease of perfusion pressure.

Whereas comparing to the control group changes were detected in the form of vicarious increase of LVF in response to hypercapnia, and the further LVF decrease in response to hypocapnia, during the hypercapnic and hypocapnic tests (Figure 3).

The Figure 3 demonstrates dopplerograms of the blood flow from the internal carotid artery during the hypercapnic and hypocapnic tests in the patients of the control group. The figure makes visible the increase of peak systolic velocity of blood flow in the internal carotid artery up to 28.6% in response to hypercapnia. This effect conforms to a sufficient functional (perfusion) reserve of *cerebral circulation. The decrease of* peripheral resistance in the brain under the influence of CO2 manifested as the decrease of peripheral resistance index in the internal carotid artery.

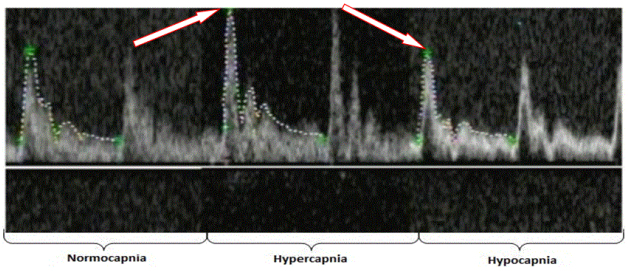

Figure 3: LVF dynamics during the hypercapnic and hypocapnic tests in the patients of the control group.

During the research by Doppler ultrasonography with the hypercapnic and hypocapnic tests the following changes were identified in the control group: the increase of LVF after the hypercapnic test to 48.8%, the increase of LVF after the hypocapnic test to 27.5% (Figure 1). The coefficient of overshoot (CO) was 1.31 ± 0.03. The normal meaning of the coefficient of overshoot is 1.24 to 1.54; the reduction under 1.2 indicates hyporesponsiveness. The meaning of the coefficient equaling 1.00 indicates areactivity [2,16,19].

During the research by Doppler ultrasonography with the hypercapnic and hypocapnic tests in patients with consequences of mild traumatic brain injuries the CO of 1.13 ± 0.04 ($p<0.01$) was identified. The increase of LVF after the hypercapnic test to 28.7% was observed, while after the hypocapnic test, the LVF showed an increase of 36.8%. Under the hypercapnic load in patients with consequences of mild traumatic brain injuries the coefficient of reactivity was lower than that of the patients in the control group (0.34 ± 0.07 and 0.46 ± 0.03 RVU respectively, $p<0.0001$).

Under the hypocapnic load in patients with consequences of mild traumatic brain injuries the coefficient of reactivity was lower than that of healthy subjects (0.44 ± 0.07 and 0.55 ± 0.04 RVU respectively, $p<0.0001$). The index of vasomotor reactivity in patients with TBI consequences was lower, than that of the control group (73.1 ± 0.05 and 97.3 ± 0.02 respectively, $p<0.0001$).

The findings are illustrated in Figure 4.

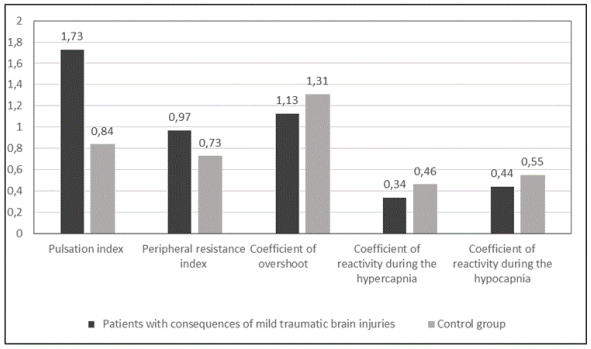

Figure 4: Correlation of hemodynamic indicators in patients with consequences of traumatic brain injuries and in healthy subjects.

A slight blood flow asymmetry was identified, increasing during hyper- and hypocapnia. The patients with consequences of mild traumatic brain injuries showed an anticipated atherosclerotic cerebral vascular disease, in the form of hemodynamically irrelevant atherosclerotic plaques. A slight blood flow asymmetry was observed, increasing during hyper- and hypocapnic tests. The increase of the contralateral blood flow was shown dependent on the injury in the mild TBI patients. A paradoxical vascular response of the common carotid artery basin was disclosed in terms of poor or delayed vascular response to hypercapnia (the increase of the LVF is naturally present) and the high and / or delayed vascular response to hypercapnia (the decrease of the LVF is naturally present) (Figure 2). In addition to the above in 52 out of 65 patients a delayed vascular response to hypercapnic and/or hypocapnic tests has been present (Figure 2). The increase of PI up to 1.73 ± 0.02; and the increase of RI up to 0.97 ± 0.02 were present in all the patients in the survey sample with consequences of traumatic brain injuries, which in turn implies liquor hypertension syndrome.

The findings are illustrated in Table 1.

	Patients with consequences of mild traumatic brain injuries (n=65) M ± m	Control group (n=30) M ± m
Pulsation index	1.73 ± 0.02***	0.84 ± 0.02
Peripheral resistance index	0.97 ± 0.02**	0.73 ± 0.05
Coefficient of overshoot	1.13 ± 0.04***	1.31 ± 0.03
Coefficient of reactivity during the hypercapnia	0.34 ± 0.05***	0.46 ± 0.03
Coefficient of reactivity during the hypocapnia	0.44 ± 0.07**	0.55 ± 0.04
Index of vasomotor reactivity	73.1 ± 0.05***	97.3 ± 0.02

Table 1: Characteristics of indicators of vascular hemodynamics in the internal carotid artery basin in the patients with consequences of mild traumatic brain injuries. *-p<0.05; ** -p<0.01;***-p<0.001.

Further, regularity has been revealed, consisting in more significant cerebral vessels reactivity on the opposite side of the injury, eventually coming of a contrecoup.

Malfunction of reactivity of vessels towards the decrease of indicators of the LVF is present in all the patients with consequences of traumatic brain injuries. A paradoxical cerebral vascular response was evident as a delayed response to the tests as carried out. The above response was accompanied by the increase of the LVF after the hypercapnic test to 28.7% (48.8% in the control group) and by the increase of the LVF after the hypocapnic test to 36.8% (27.5% in the control group). A delayed vascular response to hypercapnic and/or hypocapnic tests results, in our opinion, from reduced vessel wall elasticity on the back of microstructural damage of vessel walls and in the wake of anticipated atherosclerotic vascular disease. Such a response also exhibits a longstanding angiospasm. Liquor hypertension syndrome in such patients is, according to our reckoning, secondary and generates from a longtime vasospasm.

Conclusions

Impaired cerebral autoregulation and disturbed reactivity of vessels are evidenced in the patients with consequences of mild traumatic brain injuries in terms of decrease of linear velocity of blood flow and of increase of resistance indexes (PI and RI).

A paradoxical vascular response, arising for TBI patients, in our opinion, is related to reduced vessel wall elasticity on the back of microstructural damage of vessel walls in the wake of anticipated atherosclerotic vascular disease. The above response also exhibits a longstanding angiospasm.

References

1. Baugh CM, Stamm JM, Riley DO, Gavett BE, Shenton ME, et al. (2012) Chronic traumatic encephalopathy: neurodegeneration following repetitive concussive and subconcussive brain trauma. Brain Imaging Behav 6: 244-254.
2. Babcock L, Byczkowski T, Wade SL, Ho M, Bazarian JJ (2014) Inability of S100B to Predict Post-Concussion Syndrome in Children who Present to the Emergency Department with Mild Traumatic Brain Injury: A Brief Report . Pediatric Emergency Care 29: 458-61.
3. Roozenbeek B, Maas AI, Menon DK (2013) Changing patterns in the epidemiology of traumatic brain injury. Nat Rev Neurol 9: 231-236.
4. Walker WC, Marwitz JH, Wilk AR, Ketchum JM, Hoffman JM (2014) Prediction of headache severity (density and functional impact) after

traumatic brain injury: A longitudinal multicenter study. Cephalalgia 33: 998-1008.

5. Donovan V, Kim C, Anugerah AK, Coats JS, Oyoyo U, et al. (2014) Repeated mild traumatic brain injury results in long-term white-matter disruption. J Cereb Blood Flow Metab 34: 715-723.
6. Roozenbeek B, Maas AI, Menon DK (2013) Changing patterns in the epidemiology of traumatic brain injury. Nat Rev Neurol 9: 231-236.
7. Barbosa RR, Jawa R, Watters JM, Knight JC, Kerwin AJ, et al. (2012) Evaluation and management of mild traumatic brain injury: an Eastern Association for the Surgery of Trauma practice management guideline. J Trauma Acute Care Surg 73: S307-314.
8. Jeanne M, Allen W, Sylvia L (2014) Chronic post-traumatic headache after mild head injury. Cephalalgia 34: 174-182.
9. Eierud C, Craddock RC, Fletcher S, Aulakh M, King-Casas B, et al. (2014) Neuroimaging after mild traumatic brain injury: Review and meta-analysis. Neuroimage Clin 4: 283-294.
10. Grossman E, Ge Y, Jensen J, Babb J, Miles L, et al. (2010) Thalamus and cognitive impairment in mild traumatic brain injury: a diffusional kurtosis imaging study. J Neurotrauma 29: 2318-2327.
11. Gaidar BV, Svistov DV, Hrapov KN (1992) Semiquantitative assessment of autoregulation of cerebral blood flow in the normal. J Neurol Psychiatry 6: 38-41.
12. Miller SC, Baktash SH, Webb TS, Whitehead CR, Maynard C, et al. (2013) Risk for addiction-related disorders following mild traumatic brain injury in a large cohort of active-duty U.S. airmen. Am J Psychiatry 170: 383-390.
13. Bespalov A (1992) Effect of hypoxic hypercapnia on cerebral hemodynamics and brain tolerance to ischemia. PhD thesis 24-29.
14. Giller CA (1991) A bedside test for cerebral autoregulation using transcranial Doppler ultrasound. Acta Neurochir (Wien) 108: 7-14.
15. Vakatov D (2010) State of reactivity of cerebral vessels in the preoperative and postoperative periods in patients of elderly and senile age with brain tumors supratentorial localization. Traumatic Brain Injury 217-225.
16. Barhatov D (1992) The functionality of the blood flow in the middle cerebral artery in patients with atherosclerotic lesions of the carotid arteries. PhD thesis 26-41.
17. Jorge R, Acion L, White T, Tordesillas-Gutierrez D, Pierson R et al. (2012) White Matter Abnormalities in Veterans With Mild Traumatic Brain Injury. Am J Psychiatry 169: 1284-1291.
18. Baugh CM, Stamm JM, Riley DO, Gavett BE, Shenton ME (2012) Chronic traumatic encephalopathy: neurodegeneration following repetitive concussive and subconcussive brain trauma. Brain Imaging Behav 6: 244-254.
19. Walker WC, Marwitz JH, Wilk AR, Ketchum JM, Hoffman JM et al. (2014) Prediction of headache severity (density and functional impact) after traumatic brain injury: A longitudinal multicenter study. Cephalalgia 33: 998-1008.