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Possibilities of Application of Transcatheter Treatment of Vascular Dementia with Binswanger's Disease

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Abstract

Introduction: The research is dedicated to the main features of brain angioarchitectonics caused by the development of Binswanger's disease (BD), as well as to the effectiveness of the method of transcatheter laser revascularization of cerebral vessels in the treatment of this disease.

Materials: We examined 23 patients with BD whose age ranged from 58 to 81, mean age 78, including 15 (65.22%) men and 8 (34.78%) women. The examination included Clinical Dementia Rate (CDR), Mini-Mental State Examination (MMSE), Index Bartels (IB), laboratory examination, scintigraphy (SG), rheoencephalography (REG), Computed Tomography (CT), Magnetic Resonance Imaging (MRI) and cerebral multi-gated angiography (MUGA).

14 (60.87%) patients underwent transcatheter interventions - Test Group.

9 (39.13%) patients had conservative treatment - Control Group.

Results: Test Group: favorable clinical result - 9 (64.29%) cases; adequate clinical result - 5 (35.71%) cases; comparatively adequate and comparatively positive clinical results were not attained in any case.

Control Group: favorable and adequate clinical results were not achieved in any case; comparatively adequate clinical result was gained in 7 (77.78%) cases; comparatively positive clinical result - in 2 (22.23%) cases.

Conclusions: The method of transcatheter laser revascularization of cerebral vessels furthers natural angiogenesis, induces collateral and capillary revascularization both in ischemic areas and in closely located tissues, thereby improving cerebral blood flow. At the same time, laser energy promotes the restoration of metabolic processes in neurons. It significantly distinguishes the proposed method from conservative treatment.

Keywords: Binswanger's Disease, laser revascularization, vascular dementia treatment, subcortical lesion, brain white matter

1. Introduction

In recent decades, there has been a sufficiently rapid aging of the population, which causes an increase in the number of patients with cerebrovascular diseases complicated by neurodegenerative processes, cognitive impairment and dementia (Wilson et al., 2011; Wilson et al., 2013).

The brain is the first in the human body as far as blood supply is concerned, and therefore, its tissues are very sensitive to a decrease in blood flow and hypoxia (Gjulev et al., 2002). Under natural conditions, the intracranial arterial and capillary bed plays is especially important in the blood circulation and metabolism in the cerebral tissue (Maksimovich, 2012; Qureshi et al., 2014). When the blood supply is normal, the amount of capillaries in one cubic centimeter of the brain tissue is 3-4 thousand (Gjulev et al., 2002). Therefore, capillary blood supply disorders cause severe hemodynamic and ischemic disorders (Maksimovich, 2012).

Among neurodegenerative cerebrovascular diseases, the number of patients with Binswanger's disease (BD) increases significantly. Previously, according to various authors, BD used to be a very rare disease, but now its frequency makes 30% of all dementias (Tomimoto, 2011).

BD etiology is not fully understood (Huisa et al., 2014). Against the background of the development of CT and MRI technologies, the intensive study of the disease began in the seventies-eighties of the last century. To date, there are many studies on the visualization of structural brain changes during BD progression (Tomimoto, 2011; Pasi et al., 2011; Akiguchi et al., 2014), but insufficient attention has been paid to vascular changes in BD so far (Rosenberg et al., 2015).

The conservative treatment conducted nowadays is mainly effective in the early stages of the disease. In later stages, the white matter of the brain undergoes disseminated spread of atherosclerosis of the distal arterial and capillary bed, which causes even greater hemodynamic instability and leads to growing ischemic areas, which are often of a confluent character (Tomimoto, 2011; Rosenberg et al., 2015). Conducting conservative treatment under such conditions does not cause any marked improvement of cerebral blood flow, nor does it normalize metabolism in the white matter tissue, and therefore does not allow the desired therapeutic effect (Schneider et al., 2009).

Conducting traditional reconstructive and transcatheter interventions with BD is very difficult due to the specifics of the atherosclerotic lesion (Klopfenstein et al., 2005). Consequently, there is a need to develop new, physiological and effective BD treatment (Maksimovich, 2012).

This research aims at examining the features of brain angioarchitectonics with BD progression, as well as at studying the efficacy of the method of transcatheter laser revascularization of cerebral vessels (Maksimovich 2006) in the treatment of this disease in comparison with conservative treatment.

2. Methods

The Ethics Committee approved the whole examination and all transcatheter interventions. The consent of the examined and treated patients and their relatives was received.

We examined 23 patients whose age ranged from 58 to 81, mean age 78, including 15 (65.22%) men and 8 (34.78%) women. They had been diagnosed with BD 2 or 3 years before the examination and treatment described here.

2.1 Examination Plan

Patients were firstly examined on their admission day, then on the day of their discharge and then at intervals from six to twelve months. All patients underwent the following:

- Clinical Dementia Rating scale (CDR) was used to clinically determine dementia severity (Morris, 1993);
- Mini-Mental State Examination (MMSE) was employed to assess cognitive functions (Folstein et al., 1975; Creavin et al., 2016);
- Index Bartels Functional Evaluation: The Barthel Index (IB) was applied to to evaluate the activities of daily living (Mahoney et al., 1965);
- laboratory examination was conducted according to common in interventional neuroangiology schemes. It comprised coagulologic, biochemical and clinical tests that were taken on the admission day and after that when required (Maksimovich, 2012);
- gamma camera (Ohio Nuclear, U.S.) was used to carry out brain scintrigraphy (SG) pursuant to the classical method, in dynamic and static mode, with TC 99M Pertechnetat 555 (Maksimovich, 2012);
- "Reospektr-8" (Neurosoft, Russia) was employed to conduct rheoencephalography (REG) following the standard automated method identifying the disorders in pulse blood flow in cerebral hemispheres (Maksimovich, 2012);
- "Somatom" (Siemens), "Hi Speed" (GE), "Tomoscan" (Philips), "Apetro Eterna" (Hitachi) were made use of to accomplish CT and MRI of the brain in accordance with the classical method.
- "Advantx" (GE) apparatus was engaged to conduct brain MUGA following the classical method of transfemoral access. Omnipack 350 was introduced synchronously: 10-12 ml intra-carotidally and 7-8 ml intra-vertebrally. The beginning and the rate of its injection were paid special attention to. The direct and side projections were made in constant subtraction mode, 25 frames per second. Then the angiograms received in each phase contrast were analyzed frame by frame. Capillary density contrast was analyzed automatically at the corresponding phase by *Angio Vision 2D Perfusion* computer program, which is based on the degree of blackening of the corresponding part of the image (Maksimovich, 2012).

2.2 Selection of Patients

Patients selection criteria:

1) Disease duration of two to three years, with dementia severity level CDR-1 - CDR-2;

2) Insufficient efficacy of treatment conducted before;

3) The consent of the patients and their families to undergo the examination and treatment;

4) The patients' medical condition which should be adequate to going through the necessary examination and treatment.

Test Group: 14 (60.87%) patients who received transcatheter treatment.

Control Group: 9 (39.13%) patients that had conservative treatment. This group included patients who did not need transcatheter treatment, or they or their relatives were not willing to receive it.

2.3 Test Group

Test Group patients were treated by means of the method of transcatheter laser revascularization of cerebral vessels, which is the following. The intervention is made by transfemoral access using a set of coaxing guiding catheters. These catheters are installed in the corresponding area of intercerebral arterial bed. It is through these catheters that a flexible fiber optic light-guided instrument, the diameter of which is 25 to 100 micrometers, is taken to the affected area, where the laser treatment is performed (Maksimovich, 2004). The treatment lasts for about 20 to 40 minutes. Low-energy lasers of the visible spectrum area are used. The average power of the explosion is 20 mw (Maksimovich, 2006). To avoid the formation of thrombi, the working part of the laser instrument is permanently laved with heparin solution. When the laser treatment is completed, the patient undergoes repeated cerebral MUGA, the results of which demonstrate the level of angiogenesis and the degree of collateral and capillary bed restoration.

After the transcatheter laser treatment, the patients receive infusion and oral therapy for ten to fifteen days, which includes desagrigant, anticoagulant, vasoactive and nootropic medicine (Heparin, Warfarin, Aspirin, Pentoxifylline 100 mg, Complamin 150 mg, Inosin 200 mg, Nootropil (Piracetam) 1200 mg, Gliatilin 1000 mg). Further on, the patients have the same oral treatment received in three-month courses two times a year.

2.4 Control Group

All the patients received desagregant, anticoagulant, vasodilator and nootropic therapy including Aspirin, indirect anticoagulants (depending on the indicators of blood coagulation), Pentoxifylline 100 mg, Complamin 150 mg, Inosin 200 mg, Nootropil (Piracetam) 1200 mg (or Gliatilin 1000 mg) intravenously, dropwise, № 10-15, with subsequent transfer to pills. Then the treatment was repeated twice a year.

2.5 Results Evaluation

The results obtained comprised the following groups:

- favorable clinical result after the treatment was defined as almost complete restoration of mental and motor functions and activities of daily living (MMSE 27-30, restoration of activities of daily living IB 90-100);
- adequate clinical result was defined as incomplete restoration of mental and motor functions and activities of daily living (MMSE 21-26, restoration of activities of daily living IB 75-85);
- comparatively adequate clinical result was defined as a partial recovery of mental and motor functions and activities of daily living (MMSE 17-20, restoration of activities of daily living IB 60-70);
- comparatively positive clinical result was defined as the absence of negative dynamics with an insignificant restoration of motor recovery, intellectual abilities, with the level of activities of daily living below 60 IB points.

3. Results

3.1 The Examination Revealed:

- CDR testing detected dementia symptoms in all 23 (100%) cases: CDR-1–16 (69.57%) patients, CDR-2–7 (30.43%) patients;
- MMSE showed cognitive impairment symptoms in all 23 (100%) cases (decrease to 20–25 points was observed in 16 (69.57%) patients, to 12-19 points - in 7 (30.43%) patients);
- the testing of the activities of daily living according to IB demonstrated a decrease to 60-90 points in all 23 (100%) cases;
- high blood lipids level was identified in 20 (86.96%) cases;
- hypercoagulation was seen in 18 (78.26%) cases;

- SG showed a decrease in the blood flow in the cerebral hemispheres in all 23 (100%) cases;
- REG demonstrated decreased pulse blood volume in carotid basins in all 23 (100%) cases.

According to CT and MRI:

- cerebral cortex involutive changes along with subarachnoid space extension were found in all 23 (100%) cases;
- signs of leucoariosis were located in all 23 (100%) cases;
- signs of unocclusive hydrocephalus due to decreased brain white matter were found in all 23 (100%) cases;
- single postischemic microcysts in the brain white matter, 3-5mm in size, were detected in 2 (8.70%) cases;
- multiple fused postischemic microcysts in the brain white matter were discovered in 21 (91.30%) case;
- signs of calcium salts deposits in the vascular wall were observed in 21 (91.30%) cases.

According to MUGA, the vascular factor in BD is characterized by the development of specific arterial and capillary lesions of the intracranial bed, which were identified in all the cases:

- atherosclerotic changes in large intracranial arterial branches - 8 (34.78%) cases (Figure 1(a));
- intracranial branches deviation - all 23 (100%) cases (Figure1(a));
- diffuse atherosclerotic lesion of cerebral arteries - 23 (100%) cases (Figure 1(a));
- multiple stenotic and occlusive lesions of the terminal parts of intracranial branches - all 23 (100%) cases (Figure 1(a));
- depletion of the capillary bed in the brain white matter - all 23 (100%) cases (Figure1(b));
- multiple large (Figure (c)) and small (Figure (b), (d)) arteriovenous shunts in the brain white matter that have been caused by capillary blood flow disorders and lead to early venous arterial blood dumping were noticed in all 23 (100%) cases.

3.2 Patients Allocation:

Test Group: dementia level CDR-1, cognitive decline to 20-25 points and IB to 80 points - 10 patients; dementia level CDR-2, cognitive decline to 12-19 points and IB to 60 points - 4 patients.

Control Group - dementia to CDR-1 level, cognitive decline to 20-25 points and IB to 80 points - 5 patients; dementia at CDR-2, cognitive decline to 12-19 points and IB to 60 points - 4 patients.

3.3 Clinical Results after the Conducted Treatment

3.3.1 Test Group

A favorable immediate angiographic result demonstrating the restoration of patency and lumen of the affected vessels, as well as collateral and capillary revascularization, was achieved in all 14 cases.

In 6-12 months after the treatment (Table 1):

- favorable clinical result - 9 (64.29%) cases;
- adequate clinical result - 5 (35.71%) cases;
- comparatively adequate clinical result was not achieved in any case;
- comparatively positive clinical outcome was not gained in any case.

No negative effects were observed among the treated patients after the transcatheter laser revascularization.

3.3.1.1 Here is an Example

Patient S., female, 68 years old, three years of BD. The patient had severe arterial hypertension poorly amenable to correction, hyperlipidemia; she has suffered several transient cerebral circulatory disorders; severity of dementia equals CDR-1, MMSE- 24, IB - 85.

Cerebral MUGA revealed depletion of the capillary pattern at the level of the brain white matter (Figure 2(a)), arteriovenous shunts at the level of the brain white matter causing venous dumping of arterial blood (Figure 2(b)).

The patient underwent transcatheter laser revascularization of the front and middle cerebral arteries on both sides. Postoperative cerebral MUGA showed restoration of the distal arterial and capillary bed in the white matter of the brain (Figure 2(c)), reduction of arteriovenous shunts, and restoration of regular venous blood flow (Figure 2(d)).

SG and REG demonstrated positive dynamics of blood flow and pulse blood supply in the brain hemispheres.

The postoperative period was uneventful, and in 3 months there were no signs of dementia; MMSE - 28, IB - 100. In the distant period there were no signs of any growing cognitive disorders or signs of dementia.

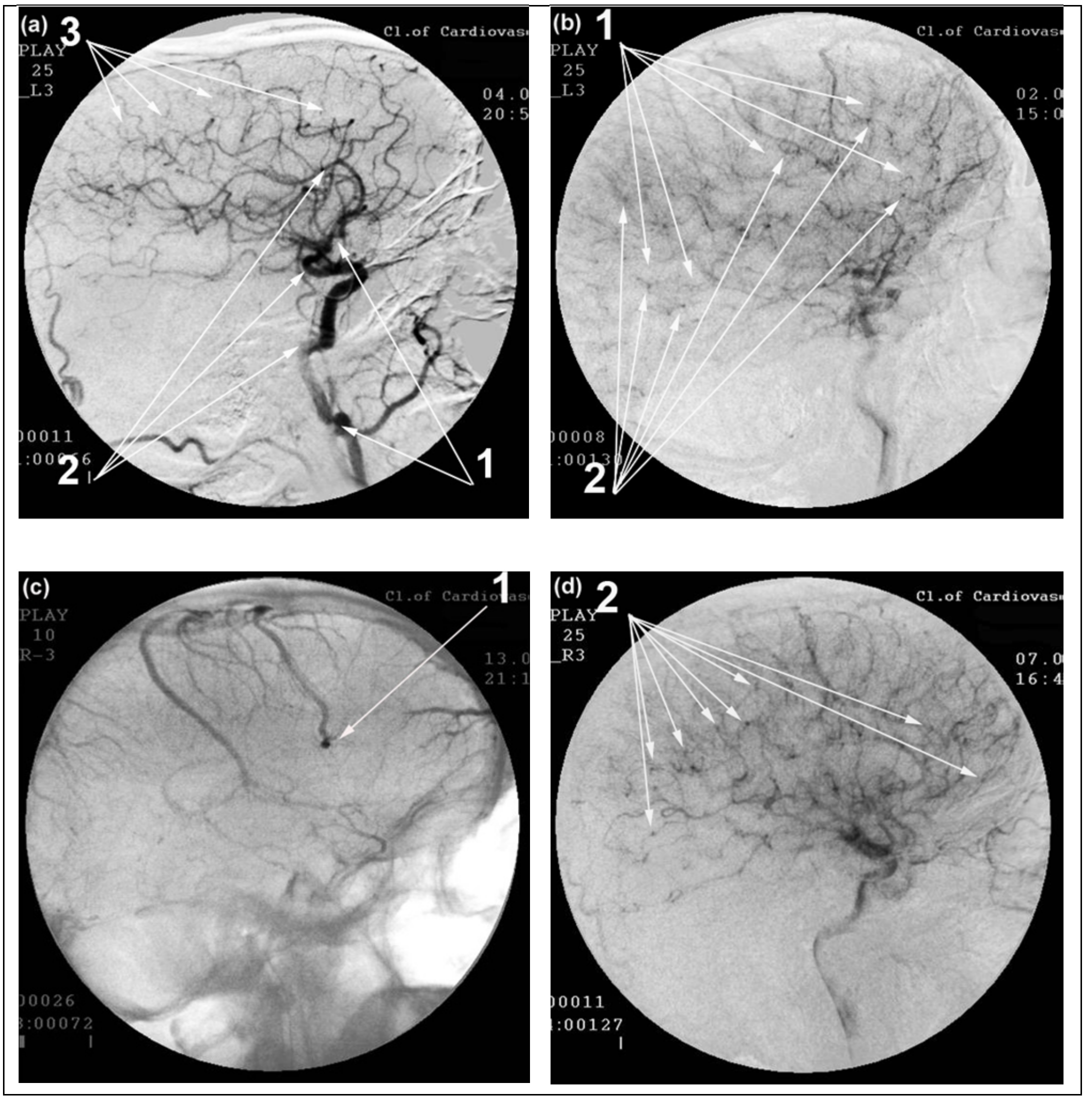

Figure 1. BD Features of Cerebral Angioarchitectonics

Lateral angiographic images. (a) arterial phase (left-sided): 1. Stenosis of large arterial branches of atherosclerotic genesis; 2. Deviation of intracranial branches; 3. Reduced subcortical capillary contrast, multiple stenotic and occlusive lesions of arterioles, precapillaries and capillaries. (b) capillary phase (left-sided): 1. Depletion of the capillary bed at the level of the white matter of the brain; 2. Arteriovenous shunts. (c) venous phase (right-sided): 1. Large arteriovenous shunt at the level of the white matter of the brain. (d) venous phase (right-sided): 2. Multiple small arteriovenous shunts at the level of the white matter of the brain.

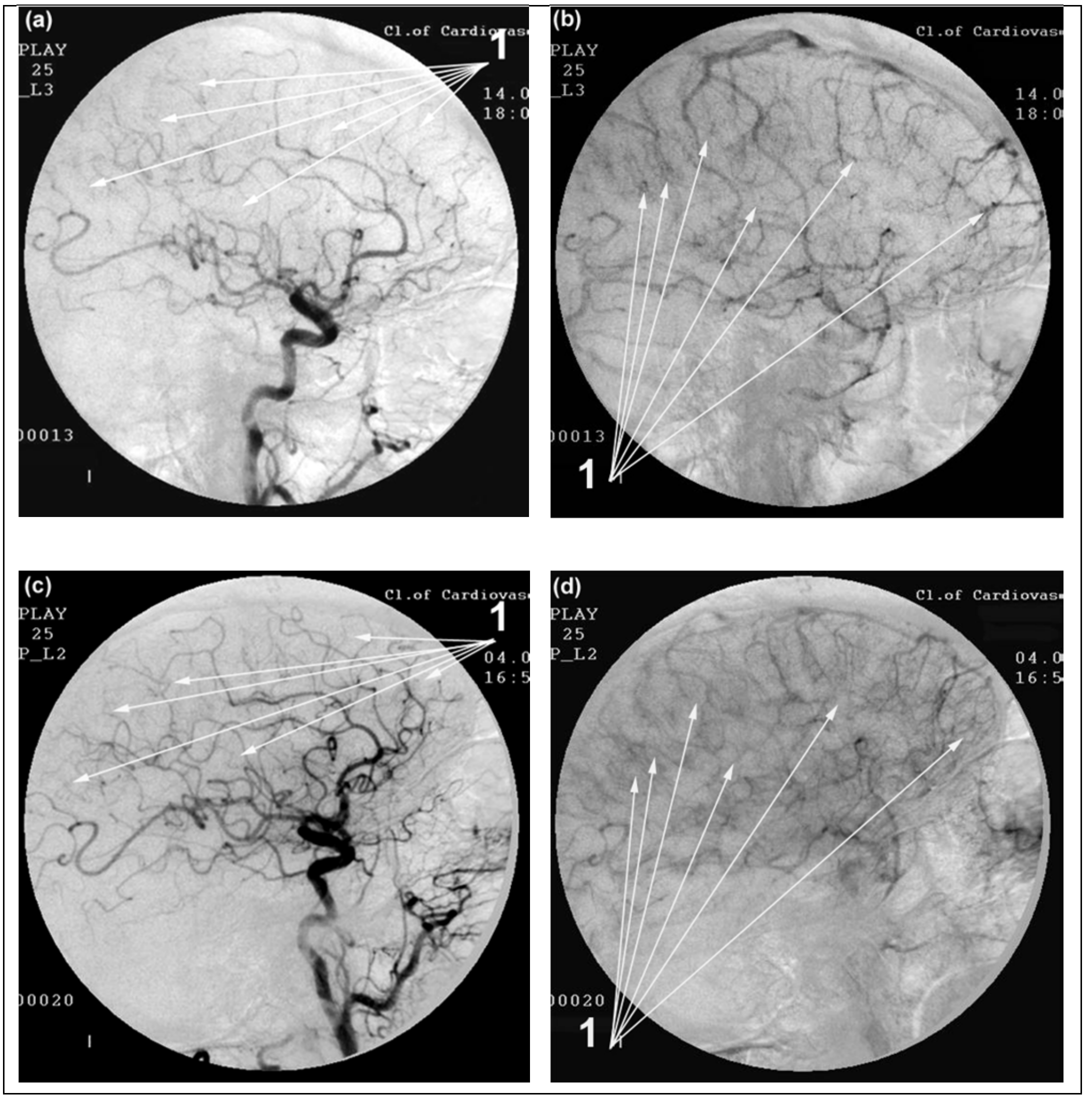

Figure 2. Patient S., female, 68 years old (CDR-1), before and after the conducted transcatheter treatment

Lateral angiographic images. (a) arterial phase (left-sided) before the intervention: 1. Depletion of the capillary bed of the brain white matter. (b) venous phase (left-sided) before the intervention: 1. Arteriovenous shunts. (c) arterial phase (left-sided) after the intervention: 1. Angiogenesis stimulation, arterial collateral and capillary bed restoration. (d) venous phase (left-sided): 1. after the intervention: 1. Decrease of multiple arteriovenous shunts.

Table 1. The Clinical Results of the Treatment.

Signs	**Test Group**	**Control Group**	**p (chi-square)**
Patients Number	14	9	
Favorable clinical result	9	0	
Adequate clinical result	5	0	0.0041
Comparatively adequate clinical result	0	7	
Comparatively positive clinical result	0	2	

The differences between the groups were identified by the analysis of the relevant contingency tables 2 × 2 by means of Pearson’s chi-square test. The corresponding values of p are shown in the last column of the table. P-value = 0.05.

3.3.2 Control Group

In 6-12 months after the treatment (Table 1):

- favorable clinical result was not achieved in any case;
- adequate clinical result was not gained in any case;
- comparatively clinical result was attained in 7 (77.78%) cases;
- comparatively positive clinical result was reached in 2 (22.23%) cases.

4. Discussion

The introduction of CT and MRI helped identify structural lesions of the brain caused by BD development (Pasi et al., 2011). Widely regarded as one of the main typical MRI signs of the disease is leucoaraiosis resulting from confluent capillary ischemic lesions of the white matter of the brain, which is found in all patients with BD (Akiguchi et al., 2014). However, leucoaraiosis symptoms can be found among individual groups of patients suffering from other forms of vascular dementia (Maksimovich, 2004, 2012). Besides, vascular dementia may be of a mixed nature. Involutive brain changes accompanied by subarachnoid space extension and unocclusive hydrocephalus also occur with many neurodegenerative diseases (Pasi et al., 2011; Akiguchi et al., 2014).

Historically, the study of cerebral vascular disorders in BD has long been conducted on the materials from anatomopathological autopsies, which led the study of this issue to only one particular direction (Qureshi et al., 2014). The data on in vivo study of the significance of the vascular factor in the etiology of this disease are quite rare (Maksimovich, 2012). In this regard, the examination of patients suffering from BD should take into account the peculiarities of angioarchitectonics in this disease.

The main feature of cerebral angioarchitectonics with BD is disseminated subcortical atherosclerotic lesion of distal intracranial arterial branches, arterioles and capillaries (Tomimoto, 2011; Rosenberg et al. 2016). In the early stages of the disease, when the symptoms of dementia and cognitive impairment are virtually absent or mild, patients feature separated areas of arterioles and capillaries reduction scattered in the white matter of the brain (Maksimovich, 2012). Further development of the disease is accompanied by a growing number of these areas, and they begin to merge, which causes leucoaraiosis (Ramos-Estebanez et al., 2011). This is often combined with multiple atherosclerotic stenosis of larger intracerebral arterial branches (Maksimovich, 2012). However, there are cases in which there is practically no diffused intracerebral atherosclerotic lesion of arterial branches, while at the same time there are some scattered subcortical focal capillary lesions, which can be of a confluent character. It may depend on the stage and duration of the disease.

Capillary lesions do not only cause tissue ischemia, but also lead to the disturbance in the venous blood outflow (Gjulev et al., 2002). Because of the reduction of the capillary bed, arterial blood cannot fully pass through the remaining functioning arterioles and capillaries, and consequently, as a compensatory reaction in respective areas of the cerebral white matter, the opening of arteriovenous shunts occurs, in which arterial blood surpluses are dumped into the venous bed (Maksimovich, 2004). This process disturbs hemodynamics even more; it also causes ischemia of tissues contributing to the development of neurodegenerative processes and subsequent mental disorders (Maksimovich, 2012). It should be noted that with BD, subcortical capillary lesions and arteriovenous shunts are disseminated in the cerebral white matter, which is the hallmark of such disturbances with other neurodegenerative diseases (Maksimovich, 2012).

Conservative treatment of BD is insufficiently effective, greatly reducing the possibility of providing medical care to patients with this severe disease (Schneider et al., 2009; Huisa et al. 2014; Rosenberg et al. 2016).). Modern medical treatment of the disease is mainly aimed at improving cerebral blood supply by means of the impact of vasodilator drugs on blood vessels and at improving tissue metabolism. Meanwhile, it does not always take into account the state of the cerebral neurovascular system and the possibility of overcoming the blood-brain barrier (BBB). Not all drugs pass through the BBB, and it should be remembered that, during BD, subcortical capillary bed afflicted by atherosclerosis reacts poorly to vasodilator effect (Rosenberg et al. 2015).

Transcatheter laser cerebral revascularization, using led tools of a small diameter, is a physiologically sound method of treatment, which has a good clinical effect in the treatment of BD. The mechanism of transcatheter low energy laser exposure lies in the powerful stimulation of the natural physiological angiogenesis. Low-energy laser endovascular impact causes rapid development of collateral and capillary revascularization of ischemic areas and closely located tissues, thereby improving cerebral blood flow and restoring metabolism in the tissue (Maksimovich, 2004, 2012). At the same time, laser energy penetrates into the cerebral tissue deeply enough, stimulates metabolic processes in neurons, boosting their energy resource due to the impact on the mitochondrial apparatus in the cells, and thus providing neuroprotection (Moskvin, 2008; Maksimovich, 2014, 2015).

The neuroprotective effect of laser energy is confirmed by many authors who conducted experimental and clinical research on extracranial laser impact on the brain with different neurodegenerative lesions (Hashmi et al., 2010; Naeser et al., 2011; Konstantinović et al., 2013; Barrett et al., 2013; Yang et at., 2010).

5. Conclusions

The method of transcateter laser revascularization of cerebral vessels is physiological and effective treatment of little injury for patients with BD. The method stimulates natural angiogenesis, thereby causing collateral and capillary revascularization of both ischemic and nearly located cerebral tissues generally improving cerebral blood flow and stimulating cell metabolism. Improving cerebral blood supply promotes reparative processes in cerebral tissues causing neurorehabilitation resulting in the reduction of mental and motor disorders, promotes dementia regression, cognitive functions restoration and improves the quality of life of patients with BD. It all significantly distinguishes the suggested method from conservative methods of treatment of this disease.

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Competing Interests Statement

The authors declare that there is no conflict of interests regarding the publication of this paper.

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