SPECIFICITY OF CEREBRAL BLOOD CIRCULATION AND COGNITIVE FUNCTION DISORDERS IN CHRONIC LUNG DISEASES AND THEIR IMPORTANCE TODAY

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Abstract: The next step was the transition to non-diffusing contrast agents, A new stage in the development of techniques based on the principle of the first passage of a contrast agent became possible after the introduction of X-ray perfusion computed tomography (PCT) into clinical practice. In recent years, comorbidity has been considered one of the most important problems in therapeutic practice.

Key words: mycocirculatory system, cerebrovascular disease, chronic obstructive pulmonary disease, clinical practice, cognitive impairment.

Introduction

In experiments on animals, data were obtained on changes in the rate of blood flow in the vessels of the brain during manipulations on the cervical sympathetic nerve. H. S. Forbes (1938) and other authors established the role of blood pressure, osmotic pressure, choline-like substances, adrenaline and CO4 levels [2]. Studies of brain microcirculation were carried out by introducing coloring agents into the carotid arteries of animals with an assessment of the time of their appearance in the retina [8]. Further studies in vivo required microscopic technology, which was first used on the brain by H. Florey and described by M. Fog [9]. Assessment of the state of the vessel diameter was carried out by photometric scanning [1]. The first experimental data on the nature of the blood flow in the superficial vessels of the brain were obtained using the "transparent skull" technique [6]. The microelectrode technique for measuring local cerebral blood flow [10], as well as the electroplethysmographic method, the thermoelectric method, and techniques with intravascular tensoresistor sensors, were widely used. Registration of blood filling of cerebral vessels based on impedance has been developed in the form of rheoencephalography and rheoplethysmography [11].

The theoretical basis of the indicator washout method was prepared by K. L. Zierler [19]. He found that the average transit time of the indicator through the tissue is the ratio of the area under the curve (A) and its first peak (H), i.e. t = A/H per minute [20]. The work of R Meier and K. L. Zierler [21] provides a mathematical justification for the indicator dilution theory and demonstrates that the average transit time is the ratio of blood volume to blood flow velocity. According to the principle of central volume, which is common to all methods for assessing tissue perfusion, these parameters are related by the ratio CBV (cerebral blood volume; cerebral blood volume) = CBF (cerebral blood

flow; cerebral blood flow)xMTT (mean transit time; mean transit time). Based on the works of K. L. Zierler, a direction was formed for studying the speed indicators of blood flow in the brain according to the dynamics of the density of non-diffusing radiopaque indicators. A great contribution was made by S. K. Hilal [22], who developed the method of X-ray densitometry for calculating the blood flow velocity in the arteries. N. A. Lassen at that time quite fully presented a review of methods for assessing cerebral blood flow in the review [23].

For a short time, the quantitative assessment of cerebral blood flow was based on X-ray videodensitometry [24]. The first use of video densitometry for assessing blood flow was with the use of analog densitometers. The method of fluorescent excitation was also used [15].

Current methods for studying tissue and cellular perfusion of the brain. Physical principles, advantages and disadvantages

L. Axel (1980) studied the theory of indicator dilution based on the principle of central volume and developed a technique for assessing tissue perfusion of the brain using dynamic PCT [27]. The latter is a series of images obtained during the passage of a bolus of a contrast agent through the brain tissue [18].

During PCT, after an intravenous injection of a contrast agent, it spreads through the venous and then through the arterial network, resulting in an increase in X-ray density on CT sections. The increase in CT density after contrast injection can be divided into two phases based on its distribution: intravascular and extravascular. At the initial stage after injection of a contrast agent, an increase in density is associated with the presence of contrast within the vascular bed. During the second stage, when the contrast passes through the basement membranes of the capillaries, there is an increase in density from both vessels and extravascular tissues. Thus, at the first stage, the increase in densitometric parameters is determined by the level of systemic and regional blood flow, and at the second stage, the increase depends on the blood volume and capillary permeability. By obtaining a series of fast sequence of images in the selected area, it is possible to measure the time of "washing out" of the contrast from the tissue after its intravenous injection. Quantitative indicators of perfusion are calculated using mathematical modeling methods that use densitometric indicators of native tissue and the vascular system.

The two most commonly used analytical methods for quantifying perfusion parameters from a dynamic series of sections are: compartment analysis and deconvolution. Both methods require data to be obtained between the "arterial entry" of the contrast agent and its "washout" to assess tissue vascularization [19].

Compartment analysis is a mathematical modeling technique based on comparing one or two parts of a volume. The first model is used to assess tissue perfusion with the presence of a contrast agent only in the vascular bed. This model is based on the Fick principle [10] and calculates tissue perfusion values based on the mass conservation principle. Perfusion values are calculated from the maximum slope (the tangent of the slope of the curve at a certain point) or the peak height of the contrast agent concentration vs. time curve. The second model is used to estimate capillary permeability and calculate blood volume. This model assumes that in addition to the intravascular space there are additional areas of accumulation of contrast agent, calculations are made using a method called Patlak analysis. This method calculates the quantitative indicators of the passage of the marker from the intravascular space to the surrounding tissues [11].

The inverse convolution method is based on the use of density-time curves to calculate the residual impulse function for tissue. The construction of curves is possible under the condition of a linear dependence of tissue density on the concentration of the contrast agent in the incoming artery at a constant blood flow. After flow correction, the height of the curve shows the amount of tissue perfusion, and the area under this curve shows the relative blood volume. An extended inverse

convolution model is used to estimate capillary permeability [3].

Both methods are generally equivalent, but differ in terms of theoretical assumptions of susceptibility to noise and movement, which is why the compartment analysis method is preferable for analyzing the blood flow of organs with a complex system of vascularization [32]. For reliable calculation and correct interpretation of perfusion parameters, certain conditions must be met: rapid administration of a contrast agent with a high iodine content - bolus, patient immobility during the study [3], knowledge of the specifics of the scanning device.

Given the unified principle of calculating the parameters of tissue blood flow, all research methods provide comparable information:

• CBV - total blood volume in the selected area of the brain tissue. This concept includes blood both in capillaries and in larger vessels - arteries, arterioles, venules and veins. This indicator is measured in milliliters of blood per 100 g of medulla (ml / 100 g); CBV is a functional parameter that reflects the mechanisms of autoregulation - a change in the diameter of blood vessels;

• CBF - the rate of passage of a certain volume of blood through a given volume of brain tissue per unit of time. CBF is measured in milliliters of blood per 100 g of medulla per minute (ml/100 g min.); is the most significant indicator of cerebral perfusion. The stability of the CBF index is maintained by the mechanisms of autoregulation, manifested in a change in the diameter of cerebral vessels depending on the level of systemic arterial pressure. So, at the limit of autoregulation mechanisms in case of pathological changes in blood pressure, the CBF index may decrease [4];

• MTT - the average time for which the blood passes through the vascular bed of the selected area of the brain tissue, measured in seconds (s). This indicator has limited specificity, since its lengthening can be caused by significant stenosis of the main arteries of the neck and head, as well as vasospasm [3].

In addition to CBF, CBV and MTT, the time to peak concentration of the contrast agent (time to peak, TTP) can also be calculated. TTR is a complex indicator consisting of two parts: the time of receipt of a contrast agent from the cubital vein to the brain and from the beginning of the entry of this substance into the brain to its maximum concentration in the studied areas of the brain. The first component directly depends on the inotropic and chronotropic functions of the heart. TTR is more sensitive to changes in the activity of the left hemisphere than the right.

Tissue blood flow is estimated from maps built for each of the parameters, as well as from their absolute and relative [5] values in the corresponding areas of the brain.

The regional transit time of the contrast agent and the rate of blood flow through a unit of vascular volume are measured. After a delay due to the passage of the indicator through the pulmonary circulation, it reaches a peak and sharply decreases with a second peak of lower amplitude due to recirculation [6]. The software of the CT scanners makes it possible to obtain curves of the density of the contrast agent as a function of time. The dynamics of tissue density after contrast injection is linearly dependent on the concentration of the contrast material [37].

A significant breakthrough in the diagnosis of cerebral microcirculation disorders in cerebrovascular pathology was achieved with the introduction of radionuclide methods into medical practice. Positron emission tomography (PET) is a technique for obtaining tomographic images and quantitative parameters of regional blood flow, including blood flow velocity, metabolic level of oxygenation and oxygen extraction, as well as cell viability, proliferation and metabolic activity of tissues . Images are obtained using biological substances labeled with radioisotopes that release positrons [4]. However, the routine use of PET is limited by the small number of tomographs, the cost and complexity of the procedure [16].

Certain hemodynamic characteristics can be obtained by single-photon emission computed tomography (SPECT), which is a non-invasive technique for assessing the distribution of a

radiopharmaceutical reflecting regional hemodynamics [5] covering the entire volume of the brain. However, this limits the possibility of obtaining quantitative data [6].

Dynamic perfusion magnetic resonance imaging (PMRI) also provides information on CBF, CBV, and MTT. The method is based on the change in the relaxation time T1 or T2 during the first passage of a contrast agent (gadolinium-based contrasts are usually used) through the capillary bed. PMRI has both advantages over PCT (better spatial resolution, no radiation exposure) and disadvantages (longer scanning time, dependence on motion artifacts, and the fact that PMRI parameters are semiquantitative [16]).

An alternative to methods for assessing cerebral blood flow based on contrast technologies today is the method of non-contrast MR perfusion - labeling of arterial spins (arterial spin labeled - ASL), which does not require the introduction of a contrast agent, since endogenous marker [17]. This method was first proposed in the early 1990s and has since been used primarily in research activities. The signal in ASL is roughly proportional to cerebral blood flow (CBF), which is significantly reduced in the core of an ischemic infarct when a large artery is affected. Preservation of CBF is often provided by the movement of blood through collateral vessels, which leads to an increase in the time of arrival of arterial blood. The principles of ASL are similar to those of CBF assessment in PET [18], since both methods are fundamentally based on the use of freely diffusible radioactive tracers, which makes it a method for assessing cellular perfusion, like PET and SPECT, and not a study method. tissue microcirculation, as methods of PCT and contrast PMRT. However, when performing PET, a radioactive tracer is injected, while when performing the ASL technique, blood itself acts as an indicator. With PET, the half-life of a radioactive tracer is approximately 2 minutes, while with ASL, when the loss of magnetization of liquid blood occurs at a magnetic field strength of 1.5 T (tesla), this indicator is about 1.2 seconds . However, when performing the procedure in conditions of high values of the magnetic field (3.0T and 7.0T), it increases to approximately 1.7 and 2.5 s, respectively, which is similar to the longitudinal relaxation time or T1 of liquid blood. The relatively rapid loss of magnetization of the "endogenous indicator" during ASL makes it possible to carry out repeated measurements within a short period of time (4-8 s), as well as to evaluate changes in CBF in response to neurological or vascular tests [19]. However, because the magnetic labeling disappears during the blood T1 relaxation time (typically within 1.2-1.8 s at the strength of the magnetic field used in clinical settings), the ASL signal may not accurately reflect CBF in ischemic, but viable zones (penumbre) [10]. Nevertheless, the technique, given the absolute safety in the absence of external contrast, with the introduction of tomographs with a higher field into medical practice (today, healthcare has mainly tomographs with a capacity of 1.5 T, less often - 3 T), probably, has serious chances for clinical application in the near future.

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