Preoperative assessment and preparation of patients with diseases affecting the central nervous system

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INTRODUCTION

The successful outcome of whatever surgical intervention on patient with coexisting brain disease has been balanced by three cornerstones:
- Understanding of pathophysiological circumstances connected to the certain brain disease;
- Influence of surgical intervention on dynamics of vascular and metabolic processes in central nervous system (CNS);
- Influence of anesthetic agents, most commonly with central depressant effects, on processes in cerebral vasculature and metabolism.

The brain has unique protection in human body. Its protection is complex, mechanical and physiological. The reason to it is small regenerative potential of cerebral structures. Solid cranial cage, blood brain barrier and cerebrospinal fluid circulation consist most important features of phylogenetically differentiated brain protection. Brain edema, intracranial pressure (ICP) increase, the blockade of cerebrospinal fluid circulation and consecutive development of hydrocephalus are the examples of protective brain mechanisms turning against vital interests of the whole body. This review will examine the most important issues of preoperative evaluation and preparation of patients with diseases affecting the central nervous system who may undergo various forms of surgery unrelated to the central nervous system disease.

PHYSIOLOGICAL ASPECTS AND THE ASSESSMENT OF CENTRAL NERVOUS SYSTEM FUNCTIONS

Circulation and metabolism of brain

Cerebral needs for oxygen and nutrients are vitally important to the whole body. That means the stability of cerebral blood flow (CBF) is conditio sine qua non for the human being to survive.
Certain facts make cerebral circulation the unique within the cardiovascular system of the human body:

1. The ability of cerebrovascular system to autonomously regulate the volume of cerebral blood flow - cerebral autoregulation;
2. The existence of blood brain barrier;
3. The influence of brain placed in incompressible cranial cavity on brain tissue perfusion.

All anesthetic agents and procedures change, more or less, intracranial vascular dynamics. Regardless of primary insult that jeopardized brain function (trauma, tumor, occlusive or hemorrhagic cerebrovascular disease), interaction between anesthetic effects and altered cerebrovascular dynamics may create the insufficient cerebral perfusion and the ischemia as a common outcome of different pathological processes within CNS².

The importance of cerebral circulation arises from the disproportion between brain weight (2% of total body weight) and its participation in cardiac output (15%), i.e. basal oxygen availability (20%)³. Cerebral circulation usually has been divided in anterior (carotid) and posterior (vertebrobasilar) confluence. At the skull base those two vascular basins are connected by circle of Willis, anatomically rather diverse anastomotic system. This arterial ring acts as a great potential reserve of intracranial collateral circulation. Considering cerebral blood flow (CBF) most important factor is so called cerebral perfusion pressure (CPP) which stands as difference between mean arterial pressure (MAP) and intracranial pressure (ICP):

\[
\text{CPP} = \text{MAP} - \text{ICP}
\]

Within broad spectrum of arterial pressure values and physiological conditions, CBF remains practically unchanged. The majority of investigators estimate that, within CPP range of 50 - 130 mmHg, there have been minimal changes of CBF. The regulation of CBF is also unique considering distribution of blood. 670 mL of total blood quantity that has been transferred to brain every minute (750 mL or 15 - 20% of cardiac output in the resting condition) comes through anterior (carotid) circulation. Barely 80 mL comes through posterior (vertebrobasilar) circulation. Difference in distribution exists even between brain gray and white matter (64mL 100g⁻¹ min⁻¹ vs. 15-20 mL 100g⁻¹ min⁻¹). (Picture 1).

Despite the fact that integrative mechanism of CBF autoregulation has not been ultimately explained, the influences of many local physical and chemical factors, with potential for vasoactivation, has been investigated.

**Carbon dioxide (CO₂)** - by its concentration in arterial blood (PaCO₂) remarkably regularly influences the change of CBF. In the range of PaCO₂ values between 20-60 mmHg CBF increases 2 - 3% for every 1 mm increment of PaCO₂⁴. The reason for this regularity has not been quite clear. Probably, the change of PaCO₂ is closely related to the change of hydrogen ion (H⁺) concentration in the blood and the brain tissue. In discrepancy to systemic circulation, acidosis evokes cerebral vasodilatation and alkalosis its vasoconstriction with decrease of CBF as consequence. It is not quite clear if this effect is permanent or just transient. Clinical consequences of correlation between PaCO₂ and CBF values have been well explained and
IX. MAINTENANCE OF CEREBRAL PERFUSION

• RECOMMENDATIONS

• A. Level I evidences
  - There are insufficient data to support a Level I recommendation for this topic.

• B. Level II evidences
  - Aggressive attempts to maintain cerebral perfusion pressure (CPP) above 70 mmHg with fluids and pressors should be avoided because of the risk of adult respiratory distress syndrome (ARDS).

• C. Level III evidences
  - CPP of < 50 mmHg should be avoided.
  - The CPP value to target lies within the range of 50–70 mm Hg. Patients with intact pressure autoregulation tolerate higher CPP values.
  - Ancillary monitoring of cerebral parameters that include blood flow, oxygenation, or metabolism facilitates CPP management.

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PICTURE 2
MAINTENANCE OF CEREBRAL PERFUSION - RECOMMENDATIONS.

utilized in neurosurgical anesthesia as - HYPERVENTILATION.

Oxygen (O2) - evokes the increase of CBF not until it diminishes below 50 mmHg (PaO2), but then the increase of CBF is quite rapid. At 30 mmHg, the value of CBF is doubled. Conversely, the increase of PaO2 above normal range provokes only mild decrease of CBF. Breathing the pure oxygen, at 2 atm, one can diminish CBF only for 1/5. It has been proven clinically that keeping the patient at PaO2 above 80 mmHg is optimal to prevent the undesirable increase of CBF5. There have been many investigational results that indicate undesirable effects of excessive PaO2 elicited by stimulating the formation of harmful superoxides and peroxides2,6,7.

Local tissue and blood physical and chemical factors - (concentration of hydrogen and potassium ions, pH, temperature). Since the famous study of Kety and Schmidt (1948) it has been known that acidosis evokes vasodilatation of cerebral vessels (increase of CBF) and alkalosis constriction (decrease of CBF)6. However, in the event of diabetic ketoacidosis those effects cannot be prevented by artificial decrease of PaCO2 (hyperventilation). Temperature is critically important for the value of CBF. Hypothermia decreases the rate of cerebral metabolism and of blood oxygen uptake. Hyperthermia acts conversely, i.e. CMRO2 and CBF increase approximately 5% for every new 0°C increment of body temperature8. As it is the case in the whole body, the importance of tissue hyperkalemia has been in signaling the appearance of cell death.

Increased intracranial pressure (ICP) is potent biomechanical factor of CBF change. It is quite obvious that pressure increase at the venous side of cerebral circulation leads to global reduction of CBF. The minimal cerebral perfusion pressure of 50 mmHg is needed to preserve adequate brain tissue oxygenation and nutrition. Why is it so in the brain, and not in systemic circulation, we can partially explain by histological structure of the brain and systemic veins. Providing minimal CBF the pressure in those veins has to be minimally greater than ambient ICP, otherwise they might have been collapsed provoking the cessation of circulation. It has been still unclear if that collapsing is ever clinically present and when? Some investigations had proven the permeance of those veins at the ICP values greater than 100 mmHg9.

The major arteries in circle of Willis are main regulators of adaptation to systemic arterial pressure changes and bear the dominant part of cerebrovascular resistance. Those arteries react promptly to systemic arterial hypertension maintaining CBF stable.

However, in time, that ability of cerebral arteries might be obsolete. Chronic hypertensia, especially patients with arteriosclerosis, have autoregulation of cerebral circulation adapted to higher values of CPP. Thereafter, they become extremely sensitive to short episodes of hypotension (cerebral infarction). Whereas systemic disturbances of circulation evoke chronic alterations in structure and quality of blood vessels (including the creation of aneurysmatic bags), they become sensible even to short episodes of hypotension (intracerebral hemorrhage). (Picture 2).

Cerebral blood flow measurement

Contemporary investigations have been directed to retrogradely placing thermodilutional catheter and Doppler ultrasound device at internal jugular vein bulb. In the meantime, the procedure has become clinically feasible in cardiovascular theatres and easily reproducible even in neurosurgical operating rooms. Transcranial NIRS (Near-Infrared Spectroscopy) has been very promising, owing to its noninvasiveness. Although semiquantitative it enables registration of CBF alterations10.

In routine practice only transcranial Doppler ultrasonography proved useful owing to its availability to measure the diameter of major arteries at skull base and the velocity of bloodstream through them. Under conditions of exact localization and the optimal “echo” angle of the vessel the velocity of bloodstream is well correlated to the global CBF in the basin of monitored artery. And, what is maybe more important, the procedure is noninvasive and relatively unexpensive11.

Intracranial pressure - monitoring and control capabilities

Intracranial hypertension is not only common complication of severe head trauma (SHT), but of whole spectrum of other intracranial pathological processes. More than half lethal outcomes after SHT have been attributed to intracranial hypertension12. Increased ICP acts undesirably by decreasing cerebral perfusion pressure (CPP) and CBF under critical values of cerebral autoregulation, i.e. 60 mmHg of mean arterial pressure, resulting in ischemic damage of brain tissue.

Continuous monitoring of ICP had been established clinically by Guillaume and Janny, more than half century ago (1951). Although more than one method of measurement had been clinically administered since the establis-
hing of procedure (epidural, subdural, parenchymal, ventricular monitoring), yet there has not been created the procedure that would measure ICP noninvasively, but accurately.

Normal values of ICP range between 5 - 15 mmHg. Values between 15 - 25 mmHg have been considered as mild form of intracranial hypertension, 25 - 40 mmHg as moderate, and values above 40 mmHg as severe form of hypertension. There is some correlation between ICP values and the prognosis of outcome after SHT, but unfortunately not for other forms of intracranial pathology.13

Clinical utility of ICP monitoring

There yet has been a controversy about threshold ICP value above which it becomes harmful for brain structures. The majority of clinicians approve only values within normal range (15 - 20 mmHg). There is no general correlation between ICP increase and the emergence of clinical neurological lesion.

As in patients with benign intracranial hypertension, relevant increase of ICP will not provoke significant neurological disruption. On the other side, head trauma may be accompanied by moderate increase of ICP and have a lethal outcome consequently. (Picture 3).

Intracranial pressure monitoring

By anatomical localization consequent methods for ICP measurement are:
- epidural,
- subdural,
- subarachnoid,
- intraventricular and
- intraparenchymatous monitoring.

Methods applied for ICP monitoring have been based on measurement of hydrostatic pressure of liquid connected with external transducer or implanted microsensor, placed directly in brain tissue, epidural or subdural space, or through catheter placed in intraventricular space.

Monitoring through intraventricular catheter has been approved as golden standard because of high accuracy and ability for therapeutical drainage of liquor. The possibility of reiterated calibrations of catheter in situ is not only one of desirable benefits. The drawbacks of this form of monitoring consequently are:
- More prevailing risk of complications, compared with other methods of monitoring (hemorrhage 1 - 2 %, infections 8 - 10 %);
- Cumbersome placement of catheter in situation of brain edema or narrow ventricles;
- Likelihood that catheter could be obstructed by blood clot or tissue debris;

Epidural, subdural and subarachnoid monitoring techniques are mutually comparable. They are less invasive than intraventricular method, so the frequency of complications is somewhat lower. The placement is easier, but their accuracy is not satisfying, they are susceptible to damaging, so they are utilized infrequently.

Fluid demands of patients with intracranial comorbidities

Patient with brain disease mostly doesn’t differ from healthy person by his daily water demands. If the patient has been oliguric it can be understood as a consequence of dehydration treatment that he had soon been admitted owing to the need for reduction of intracranial hypertension. In a patient with head trauma oliguria can indirectly indicate
the loss of significant circulatory volume of blood. In all patients with lesion of hypophysis or hypothalamus one should consider exceptional water loss, because of their tendency to develop diabetes insipidus.

**Patient’s electrolyte demands**

Diuretics have frequently been used to treat intracranial pathological processes, but that increases the loss of electrolytes. By combined treatment, applying 20% solution of mannitol and some diuretic of Henle’s loop concomitantly, excretion of sodium ion (Na⁺) will be increased 5 times, and of potassium ion (K⁺) 3 times in regard to the usage of sole mannitol solution. In addition, patient with syndrome of intracranial hypertension may lose significant quantity of K⁺ and H⁺ ions by "central" vomiting and it may culminate with hypokalemic alkalosis.

**Osmotic diuresis**

Increase of plasma osmolality and creation of osmotic gradient between brain tissue and blood has been the rational base for utilizing hypertonic solutions to diminish the brain volume and to decrease ICP. Mannitol as a 20% solution has long been primary treatment of brain edema. It doesn’t metabolize in body and doesn’t penetrate intact blood brain barrier (BBB). Dama-ged BBB elicits mannitol to penetrate into the brain tissue and to move water along new osmotic gradient. Whereas mannitol dehydrates healthy brain regions, the greater volume of damaged brain tissue is, the smaller effect of mannitol on ICP decrease will be. If the area of damaged BBB is extremely great, the "rebound" effect of mannitol may be seen. The treatment with mannitol longer than few days is irrational. Whereas mannitol doesn’t treat the origin of pathological brain process, but only the symptom - increased ICP, so after its prolonged application there may be seen the stable increase of brain tissue osmolality. Na⁺, K⁺ ions and free amino acids penetrate into the neurons and glial cells, also increasing the intracellular osmolality. The result is diminishing effect of mannitol on increased ICP.

The treatment with mannitol elicits important metabolic consequences. Osmotic diuresis elicited by mannitol evokes the excretion of significant quantities of Na⁺ and K⁺ ions. This can be disguised by their normal (even increased) plasma values in hypovolemic patient.

Diuretics of Henle’s loop (furosemide, bumetanide) have been adjuvants in forcing acute brain dehydration. Some authors even recommend them as alternative to mannitol, considering avoidance of potential undesirable effects of mannitol infusion (initial increase of ICP and acute electrolyte imbalance) after their application.

**THE EFFECTS OF SPECIAL ANESTHETIC TECHNIQUES ON CENTRAL NERVOUS SYSTEM**

Anesthetic procedures and applied anesthetic drugs significantly influence CBF and brain metabolism, directly or indirectly. Volatile anesthetics, exerting direct vasomotor action, elicit the expansion of blood vessels - vasodilation. Majority of hypnotics (barbiturates, propofol, etomidate) and opiates act in contrast - as vasoconstrictors.

Whilst barbiturates keep direct correlation between alteration of CBF and brain tissue metabolism, halogenated carbohydrates (enflurane, isoflurane, sevoflurane) violate that correlation, i.e., as CBF increase, brain metabolic processes diminish.

Intubation, respiratory depression (hypercapnia), chest wall rigidity (after admitting opiates) - are the examples of anesthetic procedures that elicit increase of ICP.

Nevertheless exact mode of anesthetic action on CNS has not been completely understood, the effects of their appliance are dose-dependent and subject to modification by other factors like: pH of blood, body temperature, coexistence of preceding neurological illness, etc.

All inhalational anesthetics generally may be considered as cerebral vasodilators, which mean having potential to increase ICP. Likewise, all inhalational anesthetic drugs, with possible exception of nitrous oxide, decrease the brain metabolic rate.

Intravenous anesthetic drugs act mostly as cerebral vasodilators, diminishing simultaneously the brain metabolic rate. The exact mechanism of cerebral vasodilatation is indirect for the majority of those agents. Depressor of the brain metabolism, as primary effect of intravenous agents, elicit decrease of CBF as a secondary consequence. The exception within hypnotic agents is ketamine that acts stimulating brain metabolism and increasing CBF consequently.

**The effects of special anesthetic techniques on central nervous system**

**Hyperventilation**

Hyperventilation is considered to be a state where the enhanced volume of air (or gas mixture) is inserted into the alveoli of lungs. Diminishing of PaCO₂ and, eventually, alkalosis of blood are the consequences of hyperventilation. Hyperventilation is one of the most important tools in the treatment of increased ICP, especially when its urgent decrease is necessary as it is the case in acute herniation of a part of the brain. The principle of hyperventilation effect is consequence of Monro-Kellie’s doctrine: "...the content of cranial cavity as a three-chamber
system". There are stable 1,600 mL (averagely) of total content within rigid cranial cavity. Three components of that content are:

- Brain tissue (84%), cerebrospinal fluid (12%) and blood (4%).

Addition of new component (hematoma, tumor, brain tissue edema) violates volume balance of three-chamber system and generates the increase of arterial pressure (Cushing’s reflex), as a first pathophysiologic reaction. Volume decrease of any system component acts as potentially compensatory mechanism.

Hyperventilation, by its physiologic effects (drop of PaCO2 and consecutive decrease of CBF), extremely rapidly ameliorates intracranial hypertension. Unfortunately, duration of this cerebral circulation protective reaction is limited. There is almost no doubt that desirable effect of decreasing volume of blood in the brain is lost within 24 - 36 h, resulting in that prolongation of hyperventilation regime over that interval would be irrational, especially having in mind the possibility of developing cerebral ischemia as adverse consequence of forced hyperventilation19. During continuous hyperventilation, after initial drop of ICP, slow, newly increase of ICP arises within 3 - 5 h and it stabilizes at the level usually lower than average values of ICP before hypocapnia commencement30.

Hyperventilation makes sense only in patients with preserved autoregulation of blood circulation. In diseases where the autoregulation has been disabled (i.e., cerebral ischemia) CBF in ischemic region commences directly to ischemia (hypoxic, chemical reduction of CBF. Possible solution could be appliance of high-frequency jet ventilation that would provide hyperventilation with less biomechanical consequences on venous blood return into the heart23.

If the hypocapnia is followed by hypoxia, cerebral vascular response to hypocapnia could be completely absent - it is the explanation for the inefficiency of spontaneous neurogenic hyperventilation of patients with the brain stem lesion in diminishing the increased ICP. Unconscious patients breathing deeply and rapidly (lesion in the mesencephalic area) decrease their own PaCO2, shifting oxygen dissociation curve "to the left" and, as a consequence, protracting the delivering of oxygen to brain tissue. The tissue hypoxia arise acting as vasodilator to brain blood vessels and preventing the ICP drop. The artificial hyperventilation (by mechanical ventilator) will compromise tissue oxygenation by the same mechanism - if it is prolonged, continuous and forced.

Severe hyperventilation (with diminishing of PaCO2 to the range of 20 - 25 mmHg) extremely rapidly decreases ICP and is applied only in urgent situations of suddenly originated vasogenic brain edema, when fast and transient reduction of ICP is necessary. In the Intensive care unit, where the prolonged treatment of intracranial hypertension is necessary, the mild hyperventilation, in the range of 30 - 35 mmHg, is more reliable because it induce tissue hypoxia more slowly and is equally efficient in long-term stabilization of ICP as extreme hypocapnia19.

Moderate hypocapnia (25 - 30 mmHg) has mostly been hazardous as prolonged treatment and would be admitted only in intraoperative procedure of routine preparation of the brain for surgical intervention where the optimal monitoring options are available: ICP, PaO2 and PaCO2. The reason is in pathophysiologic data that PaCO2 lower than 30 mmHg doesn’t decrease attained gauge of brain blood vessels any more, but diminish the velocity of circulation (increasing the cerebral venous pressure, the "time of circulation" is prolonged) accordingly25 - 26.

CONCLUSION

Considering patients with diseases affecting the central nervous system who may undergo various forms of surgery unrelated to the cranial cavity we have to resolve some key questions: what brain disease we are talking about, did we provide the consultative exam of a neurologist and/or neurosurgeon, did we explained all characteristics of the coexisting brain disease providing information about intracranial hypertension, cerebral circulation irregularities, and alterations in cerebral metabolic rate. Thereafter, we have to consider if adequate monitoring techniques are provided, including: transcranial Doppler ultrasound, ICP measurement (parenchimatous or intraventricular), monitoring of anesthesia depth (BIS), monitoring of somatosensory and/or motor evoked potentials. Does the applied anesthetic technique influence the information provided with the monitoring procedure? Finally, the therapeutic regimens on disposal for treating various forms of intracranial pathophysiologic conditions has to be consid-
erad: osmotic diuresis, hyperventilation, cerebral metabolic rate attenuation, etc.

**SUMMARY**

**PREOPERATIVNA PRIPERMA BOLESNIKA SA INTRAKRANIJALNOM PATOLOGIJOM KAO KOMORBIDITETOM**

Cič članka: Ovaj članak sažima skorašnja saznanja o preoperativnoj proceni i pripremi bolesnika sa pridruženim oboljenjima centralnog nervnog sustava. Ovi bolesnici mogu biti podvrgnuti različitim operativnim zahvaticima koji anatomski ne narušavaju integrity intrakranijalne šupljine. Diskutovane su posledice delovanja različitih fizioloških i farmakoloških činilaca na moždanu autoregulaciju i kontrolu intrakranijalnog pritiska, kao i uticaj novijih rezultata istraživanja na njihovu klinički upotrebljivost.

Pregled istraživačkih rezultata: bez obzira na vrstu operativnog zahvata, intrakranijalni patološki proces - kao komorbiditet, može značajno uticati na izbor anestetičkih lekova, tehnika i metoda praćenja vitalnih znakova. Usporavanje brzine moždanog metabolizma nije jedini mehanizam kojim anestetički lekovi ispoljavaju svoj neuroprotektivni potencijal. U definisanju optimalnog planiranja anestezije bolesnika sa nekim od intrakranijalnih komorbiddita postoje izvesni opšti principi, ali i često specifični specifičnih okolnosti. Najbolje očuvanje autoregulacije pruža kombinacija propofola i remifentanila, u sklopu totalne intravenske anestezije. Medju inhalacionim anesteticima, u klinički primjenjivim dozama, izofluran i sevofluran najbolje čuvaju autoregulaciju.

Ključne reči: centralni nervni sistem, oboljenje; anestezija, neurohirurška; procena, preoperativna

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