Preoperative assessment and preparation of patients with neurologic disorders

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Ageing of population worldwide has significant contribution as one of the major risk factor for neurodegenerative disorders. The patients with neurodegenerative as well as other neurological diseases presented the population with possible great need either of small or big surgical intervention. There are several important issues in patients with neurological diseases: the nature, disease duration, therapy, the patient’s ability to live without assistance. Neurological disease may become worst by general and regional anesthesia. Stopping therapy may lead to worsening of neurological diseases. One of the main common threat is the risk of significant cardiorespiratory complications, which is important in assessing operational risk, in preoperative preparation and in terms of postoperative recovery and outcomes of surgical treatment. This has resulted in greater preoperative care by detailed patient history evaluation and examination, patient information and informed consent. Besides the effect of the anaesthetic technique upon the course of the disease, there is also the interaction of drugs administered during anaesthesia and patient medication. Several undiagnosed diseases may be disclosed following a surgical/anaesthetic intervention.

Key words: neurological disease, preoperative preparation, anesthesia, surgery

INTRODUCTION

Patients with preexisting neurologic disease present a unique challenge to the anesthesiologist. Frequency of neurological especially neurodegenerative diseases, has increased in recent years. The reason for this is not only increasing incidence but early diagnosis and better medical therapy that many of this patients return to normal life and prolong their life span. There are over 500 different neurological diseases. Almost all neurological patients - with neurodegenerative disorders (M. Parkinson, M. Alzheimer, Amyotrophic lateral sclerosis), autoimmune disease (like multiple sclerosis, Myasthenia gravis, Guillain-Barre syndrome etc.), and the muscular dystrophies (M. Steinhart, M. Duchenne etc.), epilepsy need special preoperative preparation.

Common to most neurological diseases is the existence of muscular weakness. It is of great importance during the preoperative examination and preparation because we need to pay attention to ventilatory capacity. Also there is a high risk of developing aspiration pneumonia in these patients as a result of delayed emptying of the digestive system. It must be considered the need for preoperative nasogastric tube placement.

Depending on the duration of disease, patients may have an impaired ability to chew and swallow. They are often malnourished, so it is necessary to provide nutritional support for them, both preoperative and postoperative.

During preoperative preparation it is important to consider the following aspects of neurological diseases (Table 1).

MYASTHENIA GRAVIS

Myasthenia gravis (MG) is an autoimmune disorder with a variable weakness of skeletal muscles. MG is expressed in specific muscle groups. Skeletal muscle acetylcholine receptors are place of autoimmune attack and in a smaller number of cases are non-skeletal muscle acetylcholine receptors (as the muscle-specific receptor tyrosine kinase).1 Sign and symptoms of the disease are very versatile and can be expressed only in muscle groups as ocular sign and symptoms (ptosis, diplopia), bulbar (dysarthria, dysphagia, masticatory weakness, dysphonia), facial, respiratory muscles (ortopnea, tachypnea, respiratory failure, poor inspiratory sniff, cough), axial muscles (neck flexion, neck extension - head drop)1. It could be developed
generalized weakness with life-threatening respiratory muscle dysfunction ("myasthenic crisis")⁴.

For the symptomatic therapy is used pyridostigmine (30 - 90 mg every 4-6 h). It can lead to weakness in some patients with accompanying parasympathetic hyperactivity, bradycardia, hypersalivation, miosis, abdominal cramps⁵. The treatment of choice in these patients is plasma exchange. The short term immune therapies in addition to plasma exchange are used and intravenous immunoglobulin, immunoadsorption. For long term immunosuppressive therapy are used: prednisone, azathioprine, ciclosporin, tacrolimus, mycophenolate mofetil, (these immunosuppressants greatly reduce the use of corticosteroids)⁶. It is necessary to know all of numerous side effects of these drugs.

Besides, it is necessary to be aware of possibility of disease worsening by some drugs. For example, in most patients, using of curare and related drugs, botulinum toxin, aminoglycosides, macrolides, fluoroquinolones, quinine, procainamide, interferon - alpha, magnesium salts may lead to exacerbation. In some patients using calcium channel blockers, beta-blockers, lithium, iodinated contrast agents, statins may have effects of deterioration. D-penicillamine is contraindicated. Telithromycin can be used with great caution⁷. Pre-operatively, patients should take regularly their therapy⁸.

**Neurologist view:** the patient should take their medication.

**Anesthesiologist view:**. The great caution is directed on the response of patients to neuromuscular relaxants due to the nature of the disease and the use of anticholinesterases for treatment MG. Also these patients may be resistant to succinylcholine⁹. MG patients with or without visible symptoms of disease are extremely sensitive to nondepolarizing neuromuscular blocking drugs. Thus, intermediate acting muscle relaxants are used in these patients. The dose is 10 - 50% of the dose used in nonmyastenic patient. Patients with MG treatment should always be assessed on their sensitivity to neuromuscular blocking drugs and volatile anesthetics⁹. Sevoflurane is first drug of choice in anesthesia or together with nitrous oxide in myasthenic patients. Monitoring of neuromuscular function is important, regardless of the state of MG.

**PARKINSON’S DISEASE**

Parkinson’s disease is characterized by tremor, bradykinesia, rigidity and postural instability as a result of loss of dopaminergics neurons in the substantia nigra⁶. Diagnosis of Parkinsonism is based on the presence of at least two of the following symptoms: resting tremor, rigidity, bradykinesia and postural imbalance. Prior to diagnosis of PD, should be excluded secondary parkinsonism, for example side effects of using drugs (metoclopramide). A good response to levodopa therapy, supports the PD diagnosis.

The prevalence of the disease in industrial countries is 0.3% and after age of 60 is about 1%. Standardized incidence rates of PD are 8-18 per100 000 person-year⁷.

**Therapy aims:** to raise the level of dopamine in the basal ganglia or to reduce the effects of acetyl choline. Therefore, the main drugs in treatment are L-DOPA or dopamine receptor agonists (bromocriptine, ropinirole, pergolide, pramipexole and cabergoline). All agonists are effective in improving motor function in Parkinson’s disease. Further, and monoamine oxidase inhibitor (MAOI) (selegiline) is used, but there are some controversies about it. It prolongs the action of dopamine in the striatum⁸.

These patients have problems with swallowing and eating, pharyngeal muscle dysfunction so they are often at varying degrees of malnutrition. Ventilatory muscle weakness, poor mobility, rigidity are problems for anesthesiologists. Therefore, difficult weaning and difficult extubation are expected. Thus, these patients are susceptible to respiratory infections as well as urinary infections due to difficult micturition.
As a result of therapy, these patients have orthostatic hypotension, cardiac arrhythmias, hypotension, hypovolemia. They have muscle rigidity and tremors followed by confusion, depression, hallucinations and speech impairment. As a consequence of therapy (selegiline), there is abnormal glucose metabolism.

**Neurologist view:**
Treatment recommendations in preparation for anesthesia are:
1. Take medication (primary therapy) until the surgery
2. Continue with therapy postoperatively - levodopa half-life is 6 - 12 hours (continue postoperatively through the NGs or stoma)

**Anaesthesia view:**
Important for the anaesthesiologist is also possibility of side effects of using L-DOPA:
- Psychiatric disorders (agitation, hallucinations, mania, paranoia)
- Increased myocardial contractility and heart rate
- Orthostatic hypotension
- Gastrointestinal disturbances (nausea, vomiting)
- Anticholinergic drugs (as benzhexol) have limited efficacy and many side effects.

This reduces their usefulness.

Intravenous anesthesia: propofol is safe for use except in stereotactic procedures. Thiopental can theoretically lead to worsening symptoms of Parkinsonism due to decreasing of dopamine release. Ketamine should be avoided because of exaggerating sympathetic response, but according to the literature data in practice it was used without any major problems. Etomidate is probably safe intravenous anesthetic.

Volatile agents are probably safe except halothane, which can lead to arrhythmias.

Avoid all antidopaminergic drugs that may worsen the disease (phenothiazines, butyrophenon, metoclopramide, etc.). Avoid the combination of MAOIs and meperidine, as well as the use of narcotics. Old people, who are mostly suffering from this disease, are already very sensitive to analgesics (opioids). All analgesics may lead to muscle rigidity, especially when using a combination of MAOIs and meperidine.

**ALZHEIMER’S DISEASE**

Alzheimer’s disease is a progressive neurodegenerative disease, with characteristic degeneration of cholinergic neurons inervating the cortex amygdale and hippocampus. In these patients, there are cognitive deterioration, loss of learning ability and memory with difficulty in maintaining and sustaining attention, and further deterioration affected many other cognitive domains, and at the end the patient is completely dependend on their caregivers even with basic daily activities, like eating, bathing and toileting.

Currently the only drugs that can be used are inhibitors of acetylcholinesterase (donepezil, rivastigmine, galantamine,) and memantine as NMDA antagonist.

The drugs used in therapy are attempt to improve the quality of life of these patients.

**Neurologist view:** the patient should continue the therapy postoperatively as early as possible. Agitation, hallucinations, as in all other elderly patients should be considered.

**Anaestesiologist view:**
The cholinergic system is one of the most important modulatory neurotransmitter systems in the brain. It is not entirely clear impact of general anesthesia and anesthetics on this system in AD patients. Mainly during general anesthesia there is a desirable effect of inhaled anesthetics to reduce cholinergic transmission. On the other hand the use of inhaled anesthetics has been linked with the evolution of neurodegenerative disorders.

The use of thiopental and propofol have no effect on AD. There is no specific contraindication to the use of nondepolarizing neuromuscular blocking agents. It is noticed that the drugs in the treatment of AD can lead to prolonged acting of succinamonium and as a result have a prolonged postoperative paralysis. The use of anticholinergic drugs in small doses (atropine, scopolamine) leads to deterioration of cognitive function in adults. It is recommended to use glycopyrronium bromide because it does not pass the haemato-encephalic barrier. Further study of the influence of anesthesia on the deterioration of AD is needed. This research should help that surgery and anesthesia does not deteriorate AD.

**MULTIPLE SCLEROSIS**

Multiple sclerosis (MS) is chronic disease of the central nervous system characterized by multiple sites of demyelination of the white matter in the brain and spinal cord, but not in the peripheral nerves. Autonomic dysfunction is equally possible resulting in (orthostatic) hypotension. It is a relapsing-remitting disease that becomes secondary progressive. CNS inflammation is the primary cause of demage in MS. The real cause is not known. It is assumed that the causes are environment and genetic predisposition of hosts to activate T - cell autoimmune response against their CNS. Loss of axon and myelin are the major pathological features of MS. It is caused by direct damage by the immune cells and immune activation cascade.

The symptoms of this disease are very varied and range from anxiety and depression, impaired cognitive function, pain, motor disturbance, vertigo, visual problems, sensory disturbances, cerebellar symptoms, bowel and bladder dysfunction, brainstem symptoms, and long-term treatment. Knowing the side effects of these...
In addition to medicines in the treatment of MS there are numerous other drugs that are used in the treatment of the listed side effects. After surgical intervention, exacerbations may exist. Patients and their families should be informed about this possibility before giving consent to the surgery.

As the disease damages the neural pathways, damaged ventilating function occurs as a result of lesions in the medulla oblongata and the spinal cord. Impair ability for coughing and sputum production, especially if the paralysis of the diaphragm expressed. There is a high risk of repeated pulmonary aspiration of gastric contents.

Autonomic nervous system may also be damaged so in these patients is expressed hemodynamic instability in the perioperative period, especially if using regional anesthesia. Such hypotension may be so expressed that does not respond to treatment with intravenous fluids and vasopressors.

During preoperative preparation, should be determine the degree of neurological lesions and well-documented. Take into account the regular patient’s therapy with all the side effects.

General anesthesia is a factor of worsening MS. It must be presented to patients and their families before surgery. Inhaled anesthetics are used successfully in these patients. In all patients with muscle denervation pathology, real danger after use of succinylcholine is hyperkalemia. This can lead to cardiac arrest. Use of nondepolarizing muscle relaxants have different effects. Due to denervation and with upregulation of acetylcholine receptors there is a possibility of resistance to nondepolarizing muscle relaxant. Muscle weakness and loss of muscle mass are associated with increased susceptibility to muscle relaxants. For this reason, careful selection and dose titration of muscle relaxants is necessary in patients with MS. Muscle relaxation monitoring is recommended. Besides, prevention of hyperthermia is recommended, because of its relation with worsening MS.

Neurologist view: It should be emphasized that any stressful condition, fever/hyperpyrexia, infection even without fever, surgery and fatigue may cause exacerbations or relapses. This relapse may occur up to three months following surgery or delivery and may be three times higher than at any other time. Nevertheless pregnancy itself does not seem to affect the course of the disease. During pregnancy symptoms may even ameliorate with other immunological diseases.

Anaesthetist view: When selecting the optimal anaesthetic technique, much will depend on the respiratory function (although mostly the lower trunk is involved first) and interaction with the medication of the patient. Succinylcholine should be avoided (as in any other disease with muscle atrophy). Patients may be resistant to some non-depolarizing relaxants.

The most common fear in the peri-operative period is that exacerbations of the pre-existing deficits may depend on the anaesthetic technique used.

Although numbers of patients studied are mostly too low and no controlled studies exist, it has been suggested that general anesthesia causes less exacerbations, while epidurals and especially spinals do as cases have been reported of an acute onset of previously undiagnosed MS. This has been explained by either direct toxicity of the local anesthetic within the CSF or rather high doses of local anesthetics as with secondary C section after epidural labour analgesia. Fortunately labours may be shorter thus reducing the amount of local anesthetics (LA) required. Although the evidence for more relapses with spinal techniques is not strong, epidural seems to be less harmful than spinal anaesthesia lower LA concentrations (25% as compared to spinal) will be measured in the spinal cord white matter. In general lower concentrations are recommended than in healthy patients. Hypotension, also more likely with spinal anaesthesia may be resistant to vasopressors while causing further damage due to ischaemia.

As the blood-brain barrier may be damaged this may be an additional reason why many anaesthetists will avoid spinal anaesthesia. Dural puncture itself does not seem to cause exacerbations. Little is known about possible benefit of opioids, rather than local anaesthetics. It is also recommended not to use adrenaline. Peripheral nerve blocks do not signify any additional problem as only the CNS is involved.

**AMYOTROPHIC LATERAL SCLEROSIS**

Amyotrophic lateral sclerosis (ALS) is also known as motor neuron disease. It is a progressive degeneration of the corticospinal tract, brainstem and spinal anterior horn neurons. Reasons for the degeneration are numerous: protein aggregation, mitochondrial dysfunction, apoptosis and microglial activation. The disease develops rapidly, and about 50% of patients survive 30 months of first symptoms. Usually die due to respiratory failure. The incidence of this disease is 1.7 to 2.3 cases per 100,000 population/year.

Patients developed the following symptoms associated with impaired ability to speak, swallow, breathe, use their arms, and walk. Their treatment and care require a multidisciplinary approach. In therapy are used drugs as well as nonfarmacologic or a combination of both.

A recent review containing 139 patients with a pre-existing CNS disorder, revealed that there were no patients with new or worsening deficits after the operation performed under neuraxial anaesthesia. In this study 40 patients had MS or ALS. However, no subgroup analysis was performed.

Anesthesiologist view:

One of the characteristics of these patients is respiratory weakness that leads to dyspnoea, which occurs both in rest and during changes in position (orthopnoea). An important symptom is nocturnal hypoventilation. In the presence of signs of respiratory insufficiency, should be considered the application of ventilatory support, noninvasive or invasive. Additionally, these patients have swallowing abnormalities that lead to malnutrition and weight loss.
For them it is quite reasonable to consider the application of enteral or parenteral nutritional support.

**Epilepsy**

Epilepsy is one of the most common neurological chronic disease. The disease affected more than 50 million people worldwide. Usually begins in childhood. Every year more than 80 people per 100 000 people develop symptoms of epilepsy. Epilepsy is the name of a brain disorder characterized predominantly by recurrent and unpredictable interruptions of normal brain function, called epileptic seizures. Epilepsy is not a singular disease entity but a variety of disorders reflecting underlying brain dysfunction that may result from many different causes.

Preoperative preparation of patients must include a making plan for using of drugs. The plan is based on knowledge of the following facts:

a) the possibility that anesthetics modulate or potentiate seizure

b) an interaction of antiepileptic drugs with anesthetics
c) perioperative treatment of these patients
d) comorbidity

Anti-epileptic drugs should be used as possible until the operation. Postoperatively, they should return to therapy as early as possible. It should be keep in mind that drugs used for long term anticonvulsant therapy in the treatment of epilepsy may lead to altered activities of anesthetics and other drugs that these patients used in the treatment of other diseases. This is particularly characteristic of older generation drugs (carbamazepine, phenobarbital, phenytoin). These drugs lead to the induction of liver enzymes and thereby reduces the plasma concentration of drugs used by these patients for treatment of other diseases. Newer antiepileptic drugs have not so significant effect on the induction of liver enzymes.

These are the most important fact to bear in mind in patients with epilepsy that preparing for surgery.

**Neurologist point:** Patients treated for epilepsy should continue this therapy until the time of surgery. After-surgery medication should be given parenterally if oral intake is not desirable. Plasma levels of some substances can be measured accurately.

**Anesthesiologist view:** When general anaesthesia would be selected it should be remembered that significant drug interactions may exist between anticonvulsant drug and other drugs used during anaesthesia eg. muscle relaxants, hypnotics etc.

Phenobarbital may accelerate biotransformation of anaesthetic drugs while diphanotheine and carbamazepine may cause resistance to non-depolarizing muscle relaxants.

Some epileptogenic anaaesthesics should be avoided such as enflurane, ketamine and etomidate. Despite reports of uneventful use of these substances, it may be wise to avoid them because there are several alternatives available.

The effects of fentanyl and its analogues, especially in large doses, and propofol have also been subject of debate.

Propofol, despite reports of abnormal movements, does not have seizure activity, but depresses EEG at least similar to thiopental.

The anaesthetist should be careful with additional sedation especially in patients treated with phenobarbital. Oversedation may cause hypercapnia and acidosis also decreasing the seizure threshold. It has been suggested that spinal anaesthesia might induce a higher incidence of perioperative seizures. It is unclear whether, if true, this is caused by the higher local anaesthetic concentrations in CSF or altered CSF dynamics.

**CONCLUSION**

Neurological diseases that accompany some surgical diseases are very important for the anesthesia and postoperative recovery. These patients may have in addition to neurological damage a whole range of other diseases. They have muscle weakness, ventilatory and respiratory problems and problems with nutrition and others. In their therapy, there are a number of drugs that alter pharmacokinetic and pharmacodynamic properties of anesthetics in the body. For all elective intervention, these patients need optimally to be prepared.

Nevertheless, when faced with patients with preoperative neurological disease, many anaesthetists will consider this as a contraindication for regional anaesthesia despite a lack of controlled studies. A good preoperative examination remains mandatory while patients should be informed about technical difficulties, possible relapses and/or progress associated with the combination of stress, surgery and anaesthesia.

Patients may suffer further deficit by the anaesthetic technique selected (multiple attempts, catheters, needle trauma, vasopressor, toxicity etc.). It should be recommended that paraesthesia, adrenaline and high concentrations of local anaesthetics should be avoided at all times.

Some diseases may benefit from epidural/peripheral anaesthesia (multiple sclerosis, epilepsy, space occupying lesions, myasthenia) while for others a spinal technique may be the best choice (spine surgery, opioid-alone analgesia).

**SUMMARY**

**PREOPERATIVNA PRIPREMA I PROCENA BOLESNIKA SA NEUROLOŠKIM OBOLJENJIMA**

rizika, za preoperativnu pripremu kao i za postoperativni oporavak i ishod hirurškog lečenja. Prema tome, sveobuhvatna preoperativna priprema sa uzimanjem detaljne anamneze i sveobuhvatnim ispitivanjem uz potpunu informisanost bolesnika i naravno njegov pristanak na hiruršku intervenciju su neophodni.

Pored uticaja tehničke anestezije na tok bolesti, postoji i medjusobni uticaj lekova tokom anestezije i lekova koje koriste bolesnici u terapiji neurološkog oboljenja. Nedijagnostikovana oboljenja mogu biti otkrivena tek posle hirurške/anesteziološke intervencije.

Ključne reči: neurološka oboljenja, preoperativna priprema, anestezija, hirurgija

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