Preoperative assessment and management of patient with psychiatric comorbidity

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This article explains the most frequent psychiatric disorders such as co-morbidity in the acute surgical treatment, along with its position and importance for the surgical procedure. Besides basic features of these disorders, epidemiology and clinical expression, this article holds the latest therapeutic approach, side effects, toxicity and drug interactions, during the surgical procedure.

Frequent postoperative problems, delirium, and postoperative cognitive disorders are noted in these patients. To avoid these complications, it is recommended to use a mini-mental score examination to re-evaluate the decision and indication for high risk surgery patient.

Key words: preoperative assessment, psychiatric diseases, comorbidity

INTRODUCTION

Psychiatric illnesses and personality cognitive disorders have a significant influence on people’s lives and activities. Recent population studies from the countries with highly developed medical systems show joined and concomitant mental disorders as significant throughout all areas of the health system. Mental disorders and the treatment efficacy, being a great burden to National health systems, became a topic of a great interest.1 The role of mental disorder exceeds psychiatry itself and become more visible in area of general and primary medical practice, emergency medicine, surgery as well as in pain therapy.

Management of patients with mental disorder is of great importance in preoperative evaluation of patients with previous physical and mental trauma, cognitive and mentally induced pain disorders, related to surgical procedures. It is important that doctors recognise patients with mental disorder during preoperative assessment, because some symptoms, even somatic disorders could be related to this.3 To prevent and treat it, some psychotropic medications are used: antidepressants, anxiolytics, antipsychotics (neuroleptics), sedatives, anticonvulsants etc. In the last decade there has been more use of sedatives, neuroleptics and antidepressants in populations of much younger patients, prescribed by psychiatrists and general practitioners.

In preanesthetic and presurgical evaluations, the points of interests are neurochemical, behavioral, cognitive and emotional factors. All this is of great importance to perioperative management and pain therapy of patients, and makes it much more complex and challenging to obtain personal agreement necessary for any surgical or invasive procedure. Patients with mental disorders who hardly communicate can give inadequate anamnesis and details of their illness, symptoms and medications.4 Often, they refuse any cooperation. In postoperative periods they often develop changes in behaviour, psychomotor agitation, delirium and a whole range of cognitive disorders. If it stays as permanent, these complications make the surgical recovery harder, and challenge if not minimise the result of complete medical treatment.5 This is the reason why our goal is to obtain valid preoperative assessment of patient’s mental status and undoubted informed consent process. We also need to obtain details of psychiatric therapeutic regimen, so we can avoid drug interactions during perioperative period. Because of higher risk of developing intra and postoperative complications, such as postoperative cognitive dysfunction (POCD) and delirium in these patients, preoperative evaluation is of great importance.

EPIDEMIOLOGY OF MENTAL DISORDERS

During last two decade, major research efforts have defined incidence and prevalence of serious mental illnesses. According to data of the US Epidemiologic Catchment Area Study from 1980 - 1985, among more than 20,000 patients above 18 years, 15.7% had mental disor-
orders or addiction. Reevaluating the results, Burdoun et al. confirmed that in any six month interval during the study, 19.5% of the adult population, or one in every five, had at least one (or multiple) mental disorder. The other investigation with a US Congressional mandate, the National Comorbidity Study (NCS), in population from 15 - 45 years old, in 48 US states from 1990 - 1992, showed that 50% of people included reported chronic psychiatric illness and 30% developed it in the last 12 months. The most frequent disorders were depression, alcoholic addiction and phobias. The ageing, ethnic density and gender, socioeconomic status and geographic distribution had a prevalence trend influence. There is significant trend in affective and anxiety bipolar disorders in women population as well as, substance abuse and asocial behaviour among men. Large number of individuals with psychiatric disorders did not ask or received professional medical help, which means that most of them are not in the database of medical health system.

**DEMENTIA**

According to the International Statistical Classification of Diseases and Related Health Problems-10th Revision (ICD 10), delirium is a nonspecific organic cerebral syndrome characterized by simultaneous disturbances of consciousness and attention, perception, thinking, memory, emotion, psychomotor behaviour and the sleep-wake phase. It is manifestation of alcoholic abstinence in alcohol abusers, as delirium trenaens. Also it can be an acute confusion state, observed in more than 30% of surgical patients. It is related to the elderly, traumatised, orthopaedic patients, mostly because of pre-existing cognitive disorders, co-morbidity and dementia.

**Postoperative delirium predisposing and precipitating factors are:**

- Demographic characteristics - age >65 years and male
- Cognitive dysfunction or depression
- Functional disorder
- Sensitive disorder (visual or auditive)
- Lower oral intake
- Some medication - psychoactive substances, sedatives, narcotics, anticholinergics and alcohol
- Co-morbidity - major internal medicine and neurology diseases and disorder
- Some surgery types - high risk surgery
- ICU admission
- Pain
- Sleep deprivation
- Immobility - bead physical condition

The delirium risk assessment model shows, that the more predisposing factors and co-morbidity are involved, the lower ranked stress is enough to trigger it. The most important are visual problems, major illnesses, cognitive disorders and dehydration. Older patients risk assessment model was checked and introduced to patients who undergo hip replacement surgery. The study confirms that if many predisposing factors exist, there is a higher risk to develop postoperative delirium. To recognise predisposing and precipitating factors on time and to start treatment of postoperative delirium is of great importance. Using standardised protocol when predisposing factors are present significantly reduces the number of delirium episodes in hospitalised older patients.

**POSTOPERATIVE COGNITIVE DYSFUNCTION (POCD)**

POCD is deterioration of intellectual functions expressed by loss of memory and concentration. Damage is in the area of perception and information processing mechanisms that allow people to use their knowledge and solve the problems. Manifestation is inability in performing simple tasks, followed by confusion, hallucination and delirium, if illness is more severe. Incidence of POCD is in the wide range of 10-80%. This disorders may be transitional (up to 7 days), persistent (3-5 months) or longer. The risk factors for POCD are connected to the age and patients’ co-morbidity: psychiatric and neurological co-morbidity; addiction, illness and disease; substance abstinence; and illnesses followed with higher intracranial pressure. It is related to the type of surgery and choice of anaesthesia (cardiovascular, major abdominal, orthopaedic surgery and urology; ketamine and anticholinergic drug). Estimation of the risk of POCD can be done by testing the high risk patients in preoperative period including psychiatric high risk patients. Several tests can be used in evaluation of cognitive function. One of the oldest (1982.) and still in use is the Cognitive Failures Questionnaire (CFQ). The most often used are Abbreviated Mental Test Score (AMTS) and Mini Mental State Examination (MMSE). Test results depend mostly on intelligence, education and cognitive possibilities. It is shown that patients with pre-existing cognitive impairment in preoperative periods have a greater risk of developing POCD. Results of the 1st International Study of Postoperative Cognitive Dysfunction, on 1218 patients tested preoperatively, detected cognitive impairment in 74 patients. Further testing has been performed after 7 days when all 74 patients experienced worsening of cognitive impairment, but not uniformly for all tests (the biggest deterioration showed by Letter-Digit Coding Test). Cognitive impairment persisted after 3 month in all 74 patients, detected with all tests. Steinmetz J, associates and ISPOCD Group followed 701 surviving patients with POCD persistence after 7 days and 3 month, who underwent surgery in 1994 - 2000. All patients were followed up to August 2007, for an ave-range of 8.5 years (5.3 - 11.4 years). Results of the study show statistically significant higher mortality in groups with persistent POCD after 3 months versus groups with transient score without POCD.

**DEMENTIA**

According to the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) dementia is multiple cognitive deficits development, including memory impairment. It always goes along with at least one of the
following cognitive impairments: aphasia, apraxia, agnosia, or a disturbance in executive functions. Classification of dementia often includes some disease in ethiology origin (Alzheimer type, vascular type, head trauma, Parkinson disease, Huntington’s disease etc.). Lack of cognition or self-criticism about memory loss, or other abilities, would be usual.\textsuperscript{18} Deterioration of motor skills, frequent falls, deterioration of personal hygiene, and loss of personal belongings, behavioural disinhibition and neglect of duty, often correlate with dementia in different stages. Everything already said can be of great importance in perioperative period. Insufficient information and misinterpretation of symptoms or illness in patients, memory or speech impairment, or even inabilty to communicate are of great importance. Under those circumstances a clinician depends on heteroanamnesis from significant individuals, family members as well as on existing medical records.

Patients with early signs of dementia can already be medicated with cholinesterase inhibitor, which makes the effect of depolarizing muscle relaxant deeper and longer. Cholinesterase inhibitors can induce vagotonic and cholinergic effect of depolarizing muscle relaxant.

Searching for the drug which can have perioperative neuroprotective effect, some studies identified lidocaine as potentially neuroprotective, if infusion starts before induction in anaesthesia and proceeds the next 48 hours.\textsuperscript{20} Recently performed randomised, double-blind, placebo controlled trials, did not confirm that effect.\textsuperscript{21}

\textbf{DEPRESSION}

Depression is a frequent psychiatric disorder in populations, among 10 - 20%. It should be recognised separately and distinct from sadness and sorrow, by the quality and the duration of mood changes. Some of the patients may experience dramatic mood swings from depressive to manic episode, named bipolar disorder. There is family history and the highest incidence in the late twenties or early thirties. Women’s are affected twice as often. About 15% of them with major depression, ineffectively treated, commit suicide. Neurotransmission pathway abnormalities can be detected, and probably are the main pathophysiology mechanism of depression, but are still insufficiently investigated.

Diagnosis of depression is based on the constant presence of at least five of the following symptoms: constant, daily repeated depressed mood (sadness or empty feeling, irritability in children and adolescents), significantly reduced interest or pleasure in any activity, unintentional noticeable weight or appetite change, sleep disturbances (insomnia or excessive sleeping), restlessness, exhaustedness and lethargy, guilty or worthless feeling, concentration problem and the suicidal ideas. Organic based or mood disturbance as a reaction to death of beloved ones are excluded.\textsuperscript{22,23} Therapy recommendation includes antidepressants, selective serotonin reuptake inhibitors, antipsychotics and lithium.

\textbf{SCHIZOPHRENIA}

Disintegration of thinking process and emotional hypersensitivity is the shortest definition of serious mental disorder named schizophrenia. Typical manifestations are: acoustic illusion, obsessed or weird delusions, confused verbal communication and thinking, followed by social and professional deterioration. A child with family (parent) schizophrenia history has approximately a 10% chance to develop schizophrenia. That risk is about one percent in the general population. The peak incidence is in the late teenage period.\textsuperscript{22,23}

Schizophrenia patients are the high risk surgical patients and can developed severe hypotension and hypothermia during anaesthesia. More often they can develop postoperative mental confusion, pneumonia and ileus. Elevation of the cortizol, noradrenaline and cytokines can add to development of ileus.\textsuperscript{24} Pulmonary thromboembolism, irregular ventricular rhythm, anasarca and rabdomiolisis are seldom but still more often than in general population. Complications go along with main surgical illness worsening, use of antipsychotic drugs, drug interactions and patients’ risky life behaviour.

Ketamine, propofol and fentanyl used for anaesthesia induction lowers the postoperative confusion level in schizophrenic patient. The choice of other anaesthesia techniques, not the general, can reduce the level of complications. Epidural anaesthesia and the local anesthetic infiltration in abdominal surgery also can reduce the level of postoperative ileus.\textsuperscript{25} To reduce the level of postoperative mental complications, antipsychotic drugs should be continued.

\textbf{ANXIETY DISORDER}

Anxiety is a frequent feeling, present and persisting in the preoperative period. Often, it is possible to relieve the patient of that feeling with just talking, explanations of the procedures to follow and reassurances. Finally, premedication and intravenous sedation (eg. midazolam 2mg IV), can be induced.

Anxiety disorder can be acute or chronic, with similar symptoms presented. Moreover, it can be part of other, major psychiatric disorder symptoms: depression, somatisation and pain attacks. These symptoms, especially pain attack in panic fear can be associated with symptoms similar to myocardial infarction. Dose two illnesses can be presented with diaphoresis (excessive swathing), tachypnea and dispnea, palpitation, presyncope and existential fear. Great numbers of panic fear attacks patients, in anaesthesia already has detailed cardiology and gastroenterology examinations, without significant results.

\textbf{PSYCHOTROPIC DRUGS AND ANESTHESIA}

There is certain perioperative risks related to patients using psychiatric therapy. If oral therapy has to be stopped and there is no adequate IV substitute, worsening of chronic psychiatric disorders can occur. Moreover, there is a possibility of drug interaction between antipsychotics and anesthetics in the preoperative period.\textsuperscript{26}
Patients with lithium, monoamine oxidase inhibitors, tricyclic antidepressants as chronic therapies are at higher risk of drug interactions, worsening of the mental illness and abstinence crisis. This is the reason why these patients are classified according to American Society of Anesthesiologists as ASA 3.27

Patients mentally and physically stable, treated with selective serotonin reuptake inhibitors (SSRIs), classified as ASA 2, should be treated without disruption and risks have to be reconsidered, but probably accepted.28 Patients on a double antipsychotic and antidepressant therapy are also at higher risk. Those patients are classified as ASA 2. If therapy withdrawal and related risks are a concern, a psychiatrist has to be consulted.

Tricyclic antidepressant (TCA)

Fewer numbers of side effects and over dosage are the main reasons of SSRIs to replace TCAs. Amitriptyline, nortriptyline and imipramine are the most used TCAs in therapy of chronic pain and enuresis nocturna (involuntary urination while asleep). Sáncate amine reuptake and transferring protein competition is the mechanism of TCAs action. For the fool effect of medication, 2-4 weeks are needed. The most common side effects are similar to atropine effects: dry mouth, unclear vision, urine retention, constipation, sedation, and postural hypotension. TCAs efficacy can be increased by using competing medication (aspirin, warfarin, digoxin etc.). Overdosed, these drugs are very toxic, followed by agitation, delirium, respiratory depression and coma. Also, cardiac arrhythmias with prolonged duration of the QRS complex and QT interval are often detected. Refractory hypotension can occur. There is no need to withdraw TCAs preoperatively. Moreover, it can be dangerous to do so.29

Using of sympathomimetic drugs (adrenaline, noradrenaline) can provoke cardiovascular effects of TCAs toxicity. Use of indirect sympathomimetic drugs (ephedrine,amphetamine) can deliberate noradrenaline from the vesicles and provoke hypertensive crisis. Atropine and other anticholinergic drugs can induce postoperative confusion. Tramadol increases rise of CNS toxicity: agitation, delirium, respiratory depression and coma. High level of volatile anesthetics can induce ventricular arrhythmias. There is no specific antidote. The raising pH (alkalisation) of plasma can increase protein affinity and lowering the free drug fraction.29 It is important to know that TCAs delay gastric emptying.

Selective serotonin reuptake inhibitors (SSRIs)

SSRIs are frequently prescribed antidepressant in obsessive-compulsive disorder, panic attack etc. Drug intake disruption can provoke acute withdrawal syndrome. Mechanism of action is selective presynaptic inhibition of serotonin reuptake. Level of toxicity is much lower than TCAs. Typical side effects are gastrointestinal: nausea, vomiting, diarrhea, and CNS: insomnia, agitation, tremor, sexual disorder and headache. Bradycardia is possible but not so often cardiovascular disorder. Coronary vasoconstriction can happen to patients with ischemic heart disease. Older patients can experience anti-diuretic hormone disorder and hyponatremia. High dosage of SSRIs can induce permanently damage and reduction of the platelet aggregability. SSRIs overdose accumulates high serotonin level in synaptic cleft of pons and medulla. It is much more often in drug combination among TCAs, MAOIs, pethidine and tramadol. Toxic crisis is the manifestation named “Serotonin syndrome”. Agitation and confusion are the behaviour change; rigidity, myoclonus and hyperreflexia are the characteristic motor activity; pyrexia, diarrhea, tachycardia and unstable blood pressure are the consequences of autonomic instability etc.29 Oftena, ICU admission is needed for complete treatment of such patients in the next 24 hours. SSRIs are the inhibitors of p450 enzyme so prolong or increase the effect of some other drugs. It is related to: warfarin, teofilin, phenytoin, carbamazepine, tolbutamide and benzodiazepine (diazepam, midazolam), antihypertensive drugs type 1c (flecainide), TCAs and nonsteroidal anti-inflammatory drugs (NSAID). Special precaution is suggested with benzodiazepine, because of prolonged duration of action.

Coagulation disorder should be monitored and corrected, if needed. Serum electrolytes have to be measured in older patients, to avoid hiponatremia.

Monoamine oxidase inhibitors (MAOIs)

MAO enzyme is located in mitochondrial membrane. Its function is to inactivate (deaminates) monoamino neurotransmitter in the cytoplasm. There are two isoenzymes: A and B. Serotonin, noradrenaline and adrenaline are metabolized predominantly in CNS by enzyme MAO-A. MAO-B enzyme from non neural cells of liver and lung, metabolise aromatic amino acid phenylethylamine i methylhistamine. MAO-B takes 75% of all MAO enzyme activities. Tyramine and dogamine are the substrates for both isoenzymes (A and B).30

Indirect sympathomimetic drugs metabolized by MAO can enhance its activities and provoke fatal hypertensive crisis. Irreversible MAOIs was used previously, and for recovering this enzyme function 2-3 weeks where needed. New generations of MAO-A inhibitors drugs are reversible and selective. Antibiotic Linezolid (oxazolidinone) is a non-selective but reversible MAOI. The anti-Parkinsonian drug selegiline is a MAO-B inhibitor.31 Patients using MAOIs can undergo general anaesthesia with precautionary measures to reduce the possible risk.31 The most dangerous interactions can happen with indirect sympathomimetic drugs: ephedrine, metaraminol, amphetamine, cocaine, tyramine and some opioids. The use of these drugs (and pethidine) can provoke fatal hypertensive crisis, so it is absolutely contraindicated to use them together with MAOIs.32

Neuroleptics

Neuroleptics are drugs for use in treatment of psychosis like schizophrenia and mania. The indications are in treatment of acute hallucinations and false ideas, such as para-
noia and delusions. The main effect of this drug is to antagonize dopamine (D2) receptors in CNS. Great number of other antipsychotic drugs antagonizing other receptors as well: histamine (H1), serotonin (5HT2), muscarinic acetylcholine (mAChR) and a-adrenergic receptors.

Side effects in chronic neuroleptics use are: sedation, extrapyramidal symptoms and tardive dyskinesia (unintentional movements of the tongue, lips, face, trunk, and extremities). Seldom, some of the following side effects are present: weight gain, ginekomastia, postural hypotension, constipation, obstructive icterus and agranulocytosis. Paralytic ileus can occur in surgical patients. Chlorpromazine, haloperidol and trifluoperazine are the typical antipsychotic drugs with the highest number of extrapyramidal side effects. Clozapine, olanzapine and amisulpride are the representatives of atypical antipsychotic drugs without tendency of extrapyramidal side effects, but can evoke neutropenia (clozapine).

**Neuroleptic malignant syndrome (NMS)**

Neuroleptic malignant syndrome is a rare reaction to antipsychotic drugs, and manifested by symptoms similar to malignant hyperthermia. Patients are usually young males with symptoms of: hyperthermia, tachycardia, extrapyramidal disorders (rigidity, dystonia) and disorders of autonomic regulation (sweating, unstable blood pressure, salivation, urinary incontinence). In the case of neuroleptic malignant syndrome, patients should be transferred to ICU. Mortality is about 20%. Therapy recommendation for NMS syndrome

Early recognition is of extreme importance to reduce mortality. Immediately withdraw the neuroleptic triggers of the NMS. 100% oxygen is recommended. Intravenous Dantrolene 2-3 mg/kg doses until symptoms subside (total of 10 mg/kg/day). Supportive, intensive therapy should follow laboratory control, adequate hydration, electrolyte stabilization, temperature reduction with cooling devices and ventilatory assistance. Abrupt withdrawal of antipsychotic drugs is undesirable and potentially dangerous for the patients. Antipsychotic drugs potentiate the sedative and hypotensive effects of anesthetics, including opioids. These drugs have a significant antiemetic effect.

**Lithium**

Lithium is used for treatment of bipolar affective disorder, one of the worst forms of mood disorders, with alternating phases of depression and mania. Characteristic is a narrow therapeutic range with concentration in plasma of 0.6 - 1.0mmol/l. Lithium mimics sodium in excitative tissues. It contributes to partial opening of ion channels and accumulates in the cell interior, leading to a smaller loss of intracellular potassium, partial depolarization and reduces the release of neurotransmitters. Chronic lithium treatment leads to increased body weight, renal insufficiency and hypothyroidism. Side effects of lithium can occurs in increased concentration in plasma, above 1mmol/l.

Poisoning occurs when lithium plasma levels exceed > 1.5mmol/l. Toxic effect is aggravated by hyponatremia, diuretics and in patients with renal illness. Symptoms of poisoning include: lethargy or agitation, nausea and vomiting, thirst, polyuria, trembling hands, muscle weakness, kidney failure, ataxia, convulsions, coma and death.

Lithium poisoning therapy is symptomatic, whereas we need to correct the electrolyte disturbance and seizures. Hemodialysis can be repeated successfully in renal failure, in order to remove lithium, which is gradually entering the circulation. Lithium should not be withdrawn from treatment for minor surgical interventions. Earlier, the practice was to discontinue therapy 24 - 48 hours before major surgery. We gave up that practice because of the much higher risk of primary psychiatric illness exacerbation.

The application of Lithium potentiates the effects of neuromuscular blockade (depolarising and no-depolarising). Also lower doses of anesthetics may be required, because of decreased release of noradrenalin and dopamine in the brain stem.

Cardiovascular effects are rare, but it is possible to detect changes in the ECG. T wave can be lower or inverted. If there is discontinuity in lithium therapy, it should be continued 24 hours after the surgery.

**Drug interactions with lithium**

Thiazide diuretics reduce lithium clearance. Loop diuretics have a similar but weaker effect.

Nonsteroidal anti-inflammatory drugs can increase serum lithium to 40%. Due to the risk of worsening renal insufficiency, and potentiated lithium toxicity, these drugs should be used with caution.

ACE inhibitors not only decrease the excretion of lithium, but can provoke renal failure. Co-administration of both drugs must be monitored closely.

**CONCLUSION**

Patients with psychiatric comorbidity, schizophrenia, depression, bipolar and other disorders are population with increased risk of various complications. The preoperative treatment should pay particular attention to the therapeutic regimen used in the treatment of comorbidity. Chronic psychiatric treatment has to be continued. Abrupt withdrawal of medications can lead to worsening (exacerbation) of illness. Regular prophylactic treatment also carries risks of interaction and toxicity with anesthetics and perioperative medication. These patients have an increased risk of developing postoperative cognitive deficits, and postoperative delirium. Because of that it is suggested to perform a preoperative evaluation of cognitive status. The recommendation is to carry out a preoperative minimal examination or some other valid test, and if the score is lower than allowed, to re-evaluate decisions about the indications for surgery, regarding the risks.
SUMMARY

PREOPERATIVNA EVALUACIJA I PRIPREMA BOLENIKA SA PSIHIJATRIJSKIM KOMORBIDITETOM

U radu su prikazana najčešća psihijatrijska oboljenja, od značaja u pripremi za hiruršku intervenciju, kada ona predstavljaju komorbiditet, a akutno oboljenje zahteva hirurško lečenje. Osim osnovnih karakteristika ovih bolesti, njihove epidemiologije i kliničke slike, u radu su prikazani i terapijski režimi, njihovi neželjeni efekti, tokičnost i interakcija sa medikamentima koji se intraoperativno primenjuju.

Ukazano je i na najčešće postoperativne komplikacije kod ovih bolesnika, postoperativni delirijum i postoperativne kognitivne poremećaje. U cilju izbegavanja ovih komplikacija preporučuje se da se izvede mini-mental score examination, kako bi se re-evaluirala odluka o indikacijama za hirurško lečenje bolesnika sa povšenim rizikom za nastanak ovih komplikacija.

Ključne reči: preoperativna priprema, psihijatrijske bolesti, komorbiditet

REFERENCES


