

Cognitive Disorders Around Surgery and Its Prevention Strategies

Hassan Noor^{1,2}, Adrian Coțe^{3*}, Alexandra Micu², Valentin Pirvut^{1,2}

¹Department of Medicine, Faculty of Medicine, "Lucian Blaga" University, Sibiu, Romania. ²Hospital Medlife-Polisano, Sibiu, Romania.

³Department of Surgical Discipline, Faculty of Medicine and Pharmacy, University of Oradea, 410087 Oradea, Romania.

Abstract

One of the important complications related to surgery and anesthesia is cognitive disorders, it is necessary to think about such complications before the surgery and anesthesia and put the necessary preparations on the agenda. Lack of accuracy and lack of awareness of the factors that cause these problems can be the main cause of these problems. The purpose of this review article is to examine the causes and factors that cause cognitive problems around surgery so that by providing solutions, they can be prevented from spreading and appearing after surgery. In this study, various appropriate articles related to the topic were used, which were published between 1990 and 2022 in the field of causes of cognitive problems and prevention strategies. References for this review article are from Google Scholar, PubMed, and Science Direct were obtained. The authors used keywords including cognitive problems, psychological problems during anesthesia, after anesthesia, and surgery in these sites. In this study, the things that should be considered in anesthesia and surgery to prevent the occurrence of cognitive problems were investigated. These include: the use of neuroprotectants, psychoactive drugs, anticholinergic system, anesthesia depth, pediatrics and occurrence of problems, circadian and sleep disorders, patient privacy, blood sugar, patient's spiritual rituals, hemoglobin, electrolytes, blood pressure, capnography and oxygenation, patient position and posture, emboli, drug interactions, cardiac function, platelet activity, stress and pain, hypothermia and hyperthermia, delay in discharge, ileus and antibiotics.

Keywords: Cognitive disorders, Surgery, Cognitive problems, Psychological problems, Anesthesia

INTRODUCTION

Anesthesiology has recently been associated with psychology and neuroscience due to scientific advancements. According to the research, anesthesia, and surgery can also contribute to cognitive and behavioral issues in patients, just as brain traumas might impact a patient's neuropsychological function. In this context, crucial information regarding risk factors and preventative measures for Cognitive issues have emerged following the procedure [1].

A patient undergoing surgery has the potential to experience a variety of respiratory, cardiovascular, renal, and neuropsychological injuries at any time. Therefore, only attentive and compassionate staff members can properly manage the patient at the bedside, ensuring that the patient is not injured during the procedure and that any post-operative complications are minimized or completely resolved [2].

Medical centers that do not pay enough attention to the patient's neuropsychological risk factors and do not provide solutions have increased the prevalence of postoperative cognitive problems in their patients. Cognitive problems can develop from one day after the operation and continue for weeks and even until the end of life [2, 3]. Two general categories of cognitive disorders are postoperative delirium and postoperative cognitive dysfunction. The characteristics of postoperative delirium include: acute decrease in attention,

concentration, and failure to follow orders, poor verbal communication, hypoactive or hyperactive movements, its occurrence is from immediately after the operation to one day after [2, 4].

The prevalence of delirium is from 3 to 50% depending on the number of risk factors that the patient has. Postoperative delirium will be associated with a delay in discharge and the possibility of increased mortality and decreased cognitive level in the future [3]. Cognitive dysfunction is likely to appear in the patient from days to months after surgery and has symptoms such as impaired attention, memory,

Address for correspondence: Adrian Coțe, Department of Surgical Discipline, Faculty of Medicine and Pharmacy, University of Oradea, 410087 Oradea, Romania.
Adrian.cote@gmail.com

This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

How to cite this article: Noor H, Coțe A, Micu A, Pirvut V. Cognitive Disorders Around Surgery and Its Prevention Strategies. Arch Pharm Pract. 2024;15(1):33-9.
<https://doi.org/10.51847/OphHf7XuDm>

concentration, poor verbal communication, personality disorder or change, aggressiveness, depression, unwillingness or inability to move and work, etc. [2].

They have raised the risk factors that should be considered in the evaluation and treatment measures before the operation. The more risk factors the patient has, the more likely he will be affected by the above disorders. Therefore, efforts to reduce risk factors and implement solutions can reduce the probability of POCD. These risk factors include sick and critical patients, increasing age, especially over 70 years old, low level of cognitive function before surgery, low level of awareness and education, dementia and Alzheimer's, history of neurological or psychological disorders, hypoalbuminemia, general weakness or prolonged dehydration, metabolic disorders, history of smoking and psychoactive substances, movement disorder, abnormal electrolytes, infection and inflammation, history of cardiac, thoracic, orthopedic, and heavy surgeries [3, 5].

The purpose of this review article is to investigate the causes and factors that cause cognitive problems around surgery so that by providing solutions, they can be prevented from spreading and appearing after surgery.

MATERIALS AND METHODS

In this study, various appropriate articles related to the topic were used, which were published between 1990 and 2022 in the field of causes of cognitive problems and prevention strategies. References for this review article are from Google Scholar, PubMed, and Science Direct were obtained. The authors used keywords including cognitive problems, psychological problems during anesthesia, after anesthesia, and surgery in these sites. By studying the summaries of the articles, the researchers finally separated the articles related to the topic and extracted information from them.

RESULTS AND DISCUSSION

Things that should be considered in anesthesia and surgery to prevent the occurrence of cognitive problems were examined in this review article.

Use of Neuroprotective

Magnesium has a good neuroprotective effect. Lidocaine has neuroprotective effects, so infusion (1 mg/kg) during surgery can be effective in reducing POCD to a small extent. Glucocorticoids, such as dexamethasone, can have a beneficial effect on reducing POCD and reducing inflammation caused by surgery in the body and its subsequent complications. Intravenous progesterone has been proposed as neuroprotective and has anticonvulsant and analgesic effects in neurosurgery and sometimes in obstetrics and gynecology. Melatonin is neuroprotective, this hormone, which also has medicinal forms, plays a role in regulating the body's circadian cycle. It has been reported in some patients with delirium, depression, sleep problems, MS, and a decrease in the body's melatonin level that the use of this and

similar drugs in the night before and after surgery can be useful. Treatment with medicinal plants before the operation (of course, it is recommended not to use them one week before the operation) and after the operation can also play a role in creating better neurological conditions and reducing the complications of anesthesia and surgery [1, 6-11].

Anesthetic Drugs

The use of TIVA or propofol has shown less delirium after surgery, compared to Isoflurane and sometimes isoflurane, in children and the elderly. The use of midazolam during anesthesia or high-dose infusion, especially in sensitive patients and the elderly, can lead to a decrease in postoperative memory. Also, the occurrence of delirium caused by benzodiazepines, especially in the elderly, is seen after surgery. In addition to the fact that the elderly often suffer from a decrease in the level of cholinergic activity of the brain, benzodiazepines can also aggravate cognitive pathology with their anticholinergic effects. Haloperidol can be used instead of midazolam for the medical treatment of postoperative delirium in the elderly. The use of midazolam as a sedative in regional anesthesia should be based on the patient's needs and conditions. In sensitive patients, it is better to use a dose of 0.2 to 0.3 mg/kg and check the patient's response. In patients with respiratory problems, especially with airway disorders, psychotic patients, or with severe sleep disorders, it should be injected carefully because it can cause increased respiratory effort, fatigue, fear of the patient, hypoventilation, or exacerbation of sleep disorders after surgery. In patients with fatty liver (depending on the severity) or hyperlipidemia, there is probably a greater intensity of the response and a longer duration of effect of midazolam and nesdonal.

One of the problems that candidates for cesarean surgery face is postpartum depression (PPD). Patients with a high risk of PPD include a history of pre-natal depression, people who have recently or during pregnancy suffered mental and psychological injuries, history of PPD in previous pregnancies, the existence of nutritional, emotional, and family problems, etc. Therefore, in patients who have a higher risk of contracting the disease, magnesium injection of 4 mg/kg during induction of anesthesia and intraoperative infusion and ketamine injection during anesthesia with a dose of 0.5 to 0.8 mg/kg can significantly reduce the risk of postpartum depression, reduce attention and the use of herbal medicinal therapy after the operation such as the use of saffron, chicory, ginger, etc., strengthening the emotional support of the family, and spiritual therapy will play an important role [4, 6, 11-14].

Anticholinergic System

One of the key roles of the presence of acetylcholine in the terminals of some brain neurons, in other words, the existence of the cholinergic system in the brain, is to help maintain cognitive function. In other words, a disorder in the cholinergic system of the brain can cause cognitive impairment. Some drugs that are used during anesthesia have

anticholinergic effects, so the use of these drugs in sensitive patients such as the elderly or children increases the possibility of delirium and cognitive problems after the operation. A sudden increase or decrease in the activity of the brain's cholinergic system, especially in the long term, can have neuropsychological effects. Therefore, patients with a history of neuropsychological problems are more sensitive to changes in the cholinergic system caused by drugs, and the possibility of cognitive problems will be higher in them. Hyperactive delirium and anticholinergic syndrome are cognitive side effects of anticholinergics. For this reason, rivastigmine or donepezil are sometimes used in postoperative delirium, especially in the elderly or Alzheimer's [1, 15-18].

Depth of Anesthesia

If the depth of anesthesia during surgery is less than the surgical limit, that is, it is light anesthesia, the possibility of unconscious memory activity, REM sleep, and the possibility of awakening during surgery, recall and PTSD, phobia, and depression can be predicted for the patient in the future. On the other hand, if the level of anesthesia is too deep, the possibility of postoperative delirium increases. Therefore, accuracy in adjusting the dosage of drugs during surgery is important. In obese patients, the propofol pump infusion dose during anesthesia should be based on the patient's total weight rather than the patient's lean body mass. Therefore, in obese people who have a healthy liver and are not allergic to this drug, the drug should be injected based on the total weight of the patient. In general, the lack of these things can lead to the risk of recall: the knowledge and compassion of the staff, knowing the dosage of drugs, good communication and knowing the patient and his records, knowing the depth of anesthesia enough, controlling pain and muscle relaxation, the type and duration of surgery, Knowledge of anesthesia machine and infusion pump, coordination between personnel until the last moment, etc. [15, 16, 19, 20].

Pediatrics and Emerging Problems

Children are more likely to suffer from maladaptive behaviors due to their greater neuropsychological sensitivity; these problems are seen in 23% of children up to two weeks after the operation and sometimes they continue for several months. Maladaptive behaviors include worry, sleep disorders, aggression, stress and anxiety, disobedience to parents, nightmares, phobias, etc. The risk factors that aggravate these problems are age under 3 years, parents' worry, child's worry, stress before and after the operation, pain after the operation, length of stay and delay in discharge from the hospital, and genitourinary surgery. Use of inappropriate dose and method of anesthesia, the occurrence of respiratory or cardiac disorders before, during, or after the operation. The staff should give these important recommendations to parents after discharge to reduce the possibility of POCD and especially maladaptive behaviors: exercise and physical and mental exercises, family relaxation, use of counseling and educational methods, spiritual development of parents and children (which greatly affects

the development of thoughts), the use of proper nutrition and medicinal plants effective on nerves and memory, etc. [11, 21-23].

Sleep and Circadian Disorders

Sleep disorders include Abnormal decrease or increase in REM time (sleep in which most of the body muscles are at rest, unlike eye muscles, but the brain is active, dreaming is usually present in this phase), or NREM (sleep in which some body muscles have tone but the brain is at rest), or both during the day and night, insomnia, falling asleep late, waking up at night, nightmares, etc. Factors causing sleep disorders after surgery include postoperative pain (especially chronic pain), nausea and vomiting, narcotics and anesthetics, sleep problems and neuropsychological problems before surgery, circadian system disorder, obstructive sleep apnea, stress, and Concerns after the operation of water and electrolyte disorders, reaction to anticholinergics, lack of stability of body temperature or ambient temperature during the day and night, diabetes mellitus, etc. If we find out in the pre-operative evaluation that the patient has insomnia, they need more sedative and analgesic drugs during the operation, and failure to observe the correct dosage in these people can aggravate the disease. Allergies can cause awakening due to increased histamine release, and antihistamines can cause sleep. Weakness and immobility, depression, and lack of psychological support play a role in creating mood, sleep, and circadian disorders. Sometimes the patient needs more rest and sleep due to fatigue and complications of the disease, but too little movement and excessive fatigue aggravate the complications. Usually, in patients who have a mental history of pain, fatigue, or nausea, if we do not have a solution for them, the symptoms of the disease worsen [1, 7, 11, 24-27].

Preservation of Patient Privacy

One of the things that is in the Bill of Rights of the patient, and all countries are required to implement it, is to respect the patient's privacy. Failure to respect the patient's religion and privacy affects the patient's mood and memories and causes dissatisfaction, sleep problems, anxiety, depression, phobias, etc. [1, 28-30].

The Patient's Spiritual Manners

Patients who communicate with God, pray, and pray, have a higher morale, have less possibility of psychological damage, and recover faster physically and mentally. In today's sciences, the approach of spiritual therapy is making significant progress and recommends communication with the merciful God. Observance of spiritual rituals has an important effect on the healing process of physical, mental, and social diseases; Therefore, observing and adjusting the atmosphere and spiritual conditions of the patient can have a great effect on the improvement, discharge, and satisfaction of the patient and gaining divine satisfaction [6, 31].

Blood Sugar

During surgery, blood sugar should be kept between 100 and 180. Since glucose is one of the most crucial chemicals for brain cells to produce energy, changes in its level might have unintended consequences, particularly in sensitive patients. Neuronal activity is known to decrease in hypoglycemia, and waking up from anesthesia is severely delayed. Hyperglycemia increases the likelihood of POCD by producing inflammatory factors and metabolic reactions, especially in brain-damaged patients. In patients who have had severe physical and mental pain and stress before the operation or for any reason during the operation, due to the release of hormones such as cortisol, conglamines, growth, thyroid, etc., with an increase in blood glucose levels, a decrease in the release of insulin, and decrease the sensitivity of cells to insulin. In this situation, the possibility of hyperglycemia and the occurrence of its complications increases, especially in sensitive patients. Therefore, attention should be paid to the level of anesthesia, analgesia, physical and mental stress of the patient, and the use of drugs [11, 32].

Electrolytes

In studies, there is a significant relationship between electrolyte disorders and Alzheimer's disease, dementia, and depression. Hyponatremia is associated with neurological changes increased mortality, morbidity, and POCD. In patients with brain surgery and brain tumors and injuries, the possibility of aberrant ADH syndrome as well as the secretion of natriuretic peptide, both of which cause hyponatremia, should be considered. Neuropsychological diseases increase the possibility of hyponatremia, and some drugs used by them also have the same effect. Neuropsychological patients, children, and women are more sensitive to hyponatremia. Rapid correction of hyponatremia or hypernatremia also increases the possibility of neurological damage. Hyponatremia, hypokalemia, hypomagnesemia, and hypophosphanemia can increase the incidence of POCD. Hypokalemia and hyperkalemia, combined with acid-base disorders and changes in tissue circulation, can aggravate tissue damage [1, 11, 32].

Hemoglobin

Bleeding, dehydration, anemia, and decreased vitamin B12 levels are effective in increasing the risk of POCD [11, 33].

Blood Pressure

A change of more than 30% of normal mean arterial pressure during anesthesia and surgery can increase mortality and morbidity after surgery. The duration of hypotension and hypertension their severity during anesthesia and the cause of these two complications can express the severity of the problems caused by them after the operation. In addition to acute kidney damage myocardial damage and tissues sensitive to ischemia, cognitive damage can also occur with hypotension and hypertension after surgery. The probability of damage caused by hypotension and hypertension is higher in these people: ischemia of kidney heart and brain tissues, elderly patients, people with cardiovascular disorders,

anemias, with extensive bleeding, severe respiratory patients, or other pathological diseases. Hypotension usually occurs after spinal and epidural anesthesia. Even though body tissues have self-regulation and regulate perfusion findings, sometimes the self-regulation of tissues is mild to severely disturbed and the tissue undergoes changes in perfusion and even damage. Self-regulation disorder in the brain, which is sometimes associated with the excessive permeability of the blood-brain barrier and its disorder, can exist in the following cases: diabetes mellitus, chronic hypertension, obstructive sleep apnea, heavy smoking, hypercapnia, and patient position during surgery, neuropathy and changes in the autonomic system, vasodilators, and vasoconstrictors, inhaled anesthetics (unlike sevoflurane), head trauma, brain tumors, multiple sclerosis, chronic fatty acid feeding of high objects, schizophrenia, and psychological problems including severe depression [29, 34, 35].

Oxygenation and Capnography

Hypoxia is one of the causes of damage to neurons and tissues. Especially severe hypoxia in sensitive patients, when the pulse oximetry number shows from 95 to 100, it usually shows Pao₂ from 60 to 160 mm Hg, so Spo₂ lower than 95 should be investigated. If the pulse oximeter number is about 75, the Pao₂ is about 40 mmHg, that is, arterial and venous oxygen bar. In sensitive people with underlying diseases, especially pulmonary and cardiovascular, it is better to obtain accurate values of Pao₂ and Spo₂ with ABG. Hypercapnia causes brain vessels to dilate and increase ICP, and hypocapnia, on the contrary, if severe and long-term, can cause disorders and POCD. Sometimes acidosis and neurological disorders of cerebral perfusion increase the risk of emboli. Therefore, controlling the quality of breathing and maintaining normocapnia during surgery is important [11, 33].

Posture and Position of Patient

In high head positions, the right ventricular pressure becomes more negative compared to the veins that have been placed under surgery and at a higher height. The created gradient can cause air to enter the operated veins. In head-up positions, there will be a decrease in cerebral blood supply, CPP disorder, and cerebral blood pressure drop. In the prone position, the reduction of CPP is possible and can provide the basis for POCD. The reason for the decrease in CPP in the prone position is the decrease in the circulation of the neck vessels, the tendency to drop blood pressure due to the decrease in cardiac output, and the tendency to increase ICP or CVP. Brief damage to loss of vision is also possible due to reduced circulation and pressure on the eye tissue. Patients with risk factors in these positions are more likely to be injured. Therefore, blood pressure drop or any other risk factor of POCD in the presence of these positions can increase the probability and severity of damage [1, 36-38].

Drug Interactions

Sometimes the combination of drugs and their interactions are not considered. For example, a few cases are mentioned: In patients who take statins to reduce blood lipids, there is a rare complication of rhabdomyolysis and myopathy, which is worsened by the injection of succinylcholine. These complications are indirectly associated with an increased likelihood of POCD. Simultaneous or immediate injection of thiopental sodium with atracurium, curonium, rocuronium, and succinylcholine can form a precipitate, and if induction of anesthesia is done in the form of rapid sequence induction since this precipitate causes a delay in the drug's effect in the body, there is a possibility of being awake. The patient will be present during intubation and regurgitation. Therefore, to be sure, after the injection of Nasedonal, the intravenous line or serum should be cleaned and then the relaxing drug should be injected [11, 39].

Emboli

Vascular emboli and clots can occur during or after surgery and cause moderate to severe disorders in the tissues, including the brain. Intraoperative causes include positions, hemolytic reaction, lack of tissue circulation, severe hemodynamic changes, fat emboli in orthopedic surgeries, amniotic embolism in childbirth and cesarean section, coagulopathy disorders, etc. [11, 33, 40, 41]. Embolisms include hypoxia, decreased ETCO₂, tachypnea, wheezing, pulmonary rales, and decreased cognitive function. For patients who suffer from embolism, their other underlying diseases will also worsen, including cardiovascular, cerebral, renal, Lung, liver, and cancers, and in general, their mortality and morbidity will increase [42, 43].

Platelet Activity

In some people, the level of platelet activity is higher, which can be a risk factor for cognitive problems. In this situation, the gene expression and production of GPIIb-IIIa and P-selectin, which are located on the platelet membrane, increases. These two cause platelets to accumulate or stick to the walls of the damaged vessels. Of course, other factors such as CAMP, PAF, COX the production of thromboxane and prostaglandin, and the release of serotonin also cause the production of chelate and tissue inflammation. Hyperactive platelets can reduce brain perfusion and aggravate cognitive disorders in carotid artery disease. In addition to anticoagulant drugs that are given to prevent embolisms, some studies approach herbal drugs, but one should pay attention to the interactions of the effects of chemical and herbal drugs, especially in the amount of their use, and consult with a doctor specializing in these cases [11, 44].

Cardiac Function

Cognitive problems are more likely to occur in heart patients, especially if they have major surgeries. Enlargement of ventricles and atria, atrial fibrillation, CHF, mitral and aortic stenosis and prolapse, and right-to-left heart shunt increase the possibility of POCD [1, 11, 45].

Hypothermia and Hyperthermia

Some studies have suggested the effect of hypothermia in reducing POCD, but in others, no beneficial effect has been reported. Severe and prolonged hypothermia with reduced cardiac output and reduced tissue perfusion is not suitable for weak and sensitive patients. On the other hand, rapid rewarming can increase inflammatory factors in the body and increase POCD. Hyperthermia can also have unknown effects. Serotonin syndrome is one of the causes of hyperthermia, restlessness, hyperkinesia, tachycardia, mydriasis, seizures, diarrhea, and rhabdomyolysis. The more serotonergic drugs such as fluoxetine, sertraline, methylene blue, meperidine, fentanyl, and lithium nortriptyline are used, the more likely this syndrome will occur. Midazolam and cyproheptadine can be used in drug treatment. Decreased levels of body metabolism, such as hypothyroidism, can contribute to the exacerbation of POCD [11, 46].

Pain and Stress

Pain and stress can exacerbate POCD. One of the mechanisms is that with the increase of pain and stress, the level of cortisol and catecholamine increases and affects the brain centers. Studies have linked increased stress with memory loss after surgery. Therefore, the injection of corticosteroids should also be done according to the speed and dose of the injection and the indication. People with Cushing's, phobias, chronic anxiety and worry, and schizophrenia are more prone to memory loss after surgery. On the other hand, studies have shown that dexamethasone in the correct dose and with infusion can reduce the risk of POCD. However, the high dose and failure to comply with the indication of this drug causes an increase in POCD and even psychological complications such as mania, depression, worry, panic, behavioral changes, motor-psychological disorder, etc. The mechanism of these side effects has been considered to be changes in the activity of dopaminergic and cholinergic neurons, reduction of serotonin release, toxic effects on the hippocampus, etc. Bladder filling during anesthesia can aggravate the incidence of POCD by causing hemodynamic changes and increasing inflammatory factors in the body. In general, not emptying the bladder (after sleeping or before anesthesia) can increase the duration of REM sleep and cause stressors and inflammations in the brain [47, 48].

Delayed Discharge

One of the factors that decrease the mood level of patients, the occurrence of associated complications, and the speed of recovery, is the delay in discharge [49].

Ileus and Antibiotics

Researchers believe that the digestive-brain axis, that is, the digestive system under the guidance of physiopathological mechanisms can influence the functioning of the brain. On the other hand, millions of bacteria live as natural flora and can affect brain activity. Changes in diet, stress, and chronic and irrational use of antibiotics or probiotics can cause

abnormalities in the flora and cause cognitive changes. Excessive growth of microorganisms and failure to use antibiotics also lead to gastrointestinal infections and damage to other tissues. Postoperative ileus is a complication that increases the risk of POCD with gastrointestinal changes, delayed discharge, and hemodynamic changes. Visceral hypoperfusion can be the cause of gastrointestinal damage and an increase in systemic inflammation, followed by increased damage and disorder of other tissues and delay in the improvement of the patient's condition [1, 11, 50].

CONCLUSION

One of the important complications related to surgery and anesthesia is cognitive disorders, it is necessary to think about such complications before the surgery and anesthesia and put the necessary preparations on the agenda. Lack of accuracy and lack of awareness of the factors that cause these problems can be the main cause of these problems. The purpose of this review article is to examine the causes and factors that cause cognitive problems around surgery so that by providing solutions, they can be prevented from spreading and appearing after surgery. In this study, the things that should be considered in anesthesia and surgery to prevent the occurrence of cognitive problems were investigated. These include: the use of neuroprotectants, psychoactive drugs, anticholinergic system, anesthesia depth, pediatrics and occurrence of problems, circadian and sleep disorders, patient privacy, blood sugar, patient's spiritual rituals, hemoglobin, electrolytes, blood pressure, capnography and oxygenation, patient position and posture, emboli, drug interactions, cardiac function, platelet activity, stress and pain, hypothermia and hyperthermia, delay in discharge, ileus and antibiotics.

ACKNOWLEDGMENTS: None

CONFLICT OF INTEREST: None

FINANCIAL SUPPORT: None

ETHICS STATEMENT: None

REFERENCES

- Zarei G. Anesthesia and management of complications after surgery. *Jahad Daneshgahi*, 2017.
- Monk TG, Weldon BC, Garvan CW, Dede DE, van der Aa MT, Heilman KM, et al. Predictors of cognitive dysfunction after major noncardiac surgery. *Anesthesiology*. 2008;108(1):18-30.
- Mashour GA, Avidan MS, editors. *Neurologic outcomes of surgery and anesthesia*. Oxford University Press; 2013.
- Zhang WY, Wu WL, Gu JJ, Sun Y, Ye XF, Qiu WJ, et al. Risk factors for postoperative delirium in patients after coronary artery bypass grafting: A prospective cohort study. *J Crit Care*. 2015;30(3):606-12.
- Juliebo V, Bjørø K, Krogseth M, Skovlund E, Ranhoff AH, Wyller TB. Risk factors for preoperative and postoperative delirium in elderly patients with hip fracture. *J Am Geriatr Soc*. 2009;57(8):1354-61.
- Wang LH, Xu DJ, Wei XJ, Chang HT, Xu GH. Electrolyte disorders and aging: Risk factors for delirium in patients undergoing orthopedic surgeries. *BMC Psychiatry*. 2016;16(1):418.
- Mercolini L, Mandrioli R, Raggi MA. Content of melatonin and other antioxidants in grape-related foodstuffs: Measurement using a MEPS-HPLC-F method. *J Pineal Res*. 2012;53(1):21-8.
- Brainard J, Gobel M, Bartels K, Scott B, Koeppen M, Eckle T. Circadian rhythms in anesthesia and critical care medicine: Potential importance of circadian disruptions. *Semin Cardiothorac Vasc Anesth*. 2015;19(1):49-60.
- Perrar KM, Golla H, Voltz R. Pharmacological treatment of delirium in palliative care patients. A systematic literature review. *Schmerz*. 2013;27(2):190-8.
- Wong A, Townley SA. *Herbal medicines and anaesthesia*. Continuing education in anaesthesia, critical care & pain. 2011;11(1):14-7.
- Pardo M, Miller RD. *Basics of anesthesia*. Elsevier Health Sciences; 2017.
- Al Quwayd MN, Alluhaydan AS, Alsam AA, Alferaihi AK, Oukda AH, Alagha BB, et al. An overview on the effect of bariatric surgery on type 2 diabetes mellitus patients: Literature review. *Int J Pharm Res Allied Sci*. 2021;10(2):90-3.
- Sosnovskikh EV, Rubtsov DA, Yurievna N, Stepanova EV, Autlev KM. Reproductive function in patients with morbid obesity after bariatric surgery. *J Biochem Technol*. 2021;12(1):63-6.
- Al-Jameel O, Salhi B. Factors affecting the employees' loyalty in the mobility telecom company, Saudi Arabia. *J Organ Behav Res*. 2021;6(1):135-47.
- Blass JP, Gibson GE, Duffy TE, Plum F. Cholinergic dysfunction: A common denominator in metabolic encephalopathies. *Cholinergic Mech Adv Behav Biol*. 1981;9:21-8.
- Mashour GA, Avidan MS. Psychological trajectories after intraoperative awareness with explicit recall. *Anesth Analg*. 2014;119(1):1-3.
- Alomari SA, Alfaqih AS, Alzahrani KA, Alzahrani KH, Alzahrani KM, Abdulrahman K, et al. An overview of the role of surgery in resectable pancreatic tumors. *Pharmacophore*, 2021;12(4):86-91.
- Alruwaili NR, Al Senan AK, Alqurayn MN, Bukannan AY, Baali NM, Almuzaini AM, et al. An overview of the diagnosis and management of avascular necrosis: Literature review. *Int J Pharm Res Allied Sci*. 2021;10(1):15-8.
- Postol OL, Shchadilova IS. Using neuro-stimulating physical exercises to restore cognitive functions in the correction of the post-COVID syndrome. *J Biochem Technol*. 2022;13(3):26-31.
- Ceylan C, Tacoglu C, Kartal H. Analysis of the factors affecting organizational commitment: An empirical application. *J Organ Behav Res*. 2021;6(1):6-20.
- Abu-Shahwan I. Effect of propofol on emergence behavior in children after sevoflurane general anesthesia. *Paediatr Anaesth*. 2008;18(1):55-9.
- Mehra R, Stone KL, Varosy PD, Hoffman AR, Marcus GM, Blackwell T, et al. Nocturnal arrhythmias across a spectrum of obstructive and central sleep-disordered breathing in older men: Outcomes of sleep disorders in older men (MrOS sleep) study. *Arch Intern Med*. 2009;169(12):1147-55.
- Mezhidov BS, Belyaeva AA, Bimarzaev KS, AM AS, Shekhshebekova MG, Baklanov IS, et al. Prospects for creating computer- and MRI-based 3d models of internal organs in emergency surgery and resuscitation. *Pharmacophore*. 2021;12(1):8-14.
- Otani K, Kurz RS. The impact of nursing care and other healthcare attributes on hospitalized patient satisfaction and behavioral intentions. *J Healthc Manag*. 2004;49(3):181-96.
- Finan PH, Goodin BR, Smith MT. The association of sleep and pain: An update and a path forward. *J Pain*. 2013;14(12):1539-52.
- Franks NP. General anaesthesia: From molecular targets to neuronal pathways of sleep and arousal. *Nat Rev Neurosci*. 2008;9(5):370-86.
- Romero-Martínez N, Ramos-Zambrano E, Osorio-Ruiz A, Martínez-Ayala AL. Main mechanisms of action of policosanol in animal and plant cells. *Int J Pharm Res Allied Sci*. 2021;10(2):10-20.
- Amini A, Tabrizi JS, Shaghaghi A. The status of observing patient rights charter in outpatient clinics of Tabriz university of medical sciences: Perspectives of health service clients. *Iran J Med Educ*. 2013;13(7):611-22.
- Seybold KS, Hill PC. The role of religion and spirituality in mental and physical health. *Curr Dir Psychol Sci*. 2001;10(1):21-4.
- Ranganadhareddy A, Varghese R. A review of PHB production by cyanobacteria and its applications. *J Biochem Technol*. 2022;13(4):50-3.
- Yangarber-Hicks N. Religious coping styles and recovery from serious mental illnesses. *J Psychol Theol*. 2004;32(4):305-17.

32. Niazi AA. Postoperative cognitive function and controlled hypotensive anesthesia in patients undergoing septoplasty. *Egypt J Anaesth.* 2016;32(1):61-6.
33. Morgan Jr GE, Mikail MS. Clinical anesthesiology. In *Clinical anesthesiology 1996* (pp. 881-881).
34. Mosleh S, Masoudi Alavi N, Fatemi N, Haghighat S. Procedural pain and management of this pain in trauma patients in emergency department. *Nurs Midwifery J.* 2018;15(12):902-10.
35. Deiner S, Chu I, Mahanian M, Lin HM, Hecht AC, Silverstein JH. Prone position is associated with mild cerebral oxygen desaturation in elderly surgical patients. *PLoS One.* 2014;9(9):e106387.
36. Leibovitch I, Casson R, Laforest C, Selva D. Ischemic orbital compartment syndrome as a complication of spinal surgery in the prone position. *Ophthalmology.* 2006;113(1):105-8.
37. Bithal PK, Pandia MP, Dash HH, Chouhan RS, Mohanty B, Padhy N. Comparative incidence of venous air embolism and associated hypotension in adults and children operated for neurosurgery in the sitting position. *Eur J Anaesthesiol.* 2004;21(7):517-22.
38. Cho SY, Kim SJ, Jeong CW, Jeong CY, Chung SS, Lee J, et al. Under general anesthesia arginine vasopressin prevents hypotension but impairs cerebral oxygenation during arthroscopic shoulder surgery in the beach chair position. *Anesth Analg.* 2013;117(6):1436-43.
39. Maghawry KM, El-Agamy AE, Tahir WI, Zein AF. Cerebral oxygen saturation monitoring during hypotensive anesthesia in shoulder arthroscopy: A comparative study between dexmedetomidine and esmolol. *Egypt J Anaesth.* 2015;31(1):43-52.
40. Mirski MA, Lele AV, Fitzsimmons L, Toung TJ. Diagnosis and treatment of vascular air embolism. *Anesthesiology.* 2007;106(1):164-77.
41. Stellos K, Katsiki N, Tatsidou P, Bigalke B, Laske C. Association of platelet activation with vascular cognitive impairment: Implications in dementia development? *Curr Vasc Pharmacol.* 2014;12(1):152-4.
42. Girard F, Ruel M, McKenty S, Boudreault D, Chouinard P, Todorov A, et al. Incidences of venous air embolism and patent foramen ovale among patients undergoing selective peripheral denervation in the sitting position. *Neurosurgery.* 2003;53(2):316-9.
43. Hering R, Wrigge H, Vorwerk R, Brensing KA, Schröder S, Zinserling J, et al. The effects of prone positioning on intraabdominal pressure and cardiovascular and renal function in patients with acute lung injury. *Anesth Analg.* 2001;92(5):1226-31.
44. Nurtjahja-Tjendraputra E, Ammit AJ, Roufogalis BD, Tran VH, Duke CC. Effective anti-platelet and COX-1 enzyme inhibitors from pungent constituents of ginger. *Thromb Res.* 2003;111(4-5):259-65.
45. Makaryus R, Lee H, Yu M, Zhang S, Smith SD, Rebecchi M, et al. The metabolomic profile during isoflurane anesthesia differs from propofol anesthesia in the live rodent brain. *J Cereb Blood Flow Metab.* 2011;31(6):1432-42.
46. Broadbent E, Petrie KJ, Alley PG, Booth RJ. Psychological stress impairs early wound repair following surgery. *Psychosom Med.* 2003;65(5):865-9.
47. Ahn HJ, Chung SK, Dhong HJ, Kim HY, Ahn JH, Lee SM, et al. Comparison of surgical conditions during propofol or sevoflurane anaesthesia for endoscopic sinus surgery. *Br J Anaesth.* 2008;100(1):50-4.
48. Samir GM, Gerges-Fahmy N, Labib HA. The effects of adding lidocaine hydrochloride nasal spray (10%) to xylometazoline nasal drops (0.1%) in functional endoscopic sinus surgery: A comparative study. *Ain Shams J Anesthesiol.* 2016;9(4):598.
49. Clarke G, Grenham S, Scully P, Fitzgerald P, Moloney RD, Shanahan F, et al. The microbiome-gut-brain axis during early life regulates the hippocampal serotonergic system in a sex-dependent manner. *Mol Psychiatry.* 2013;18(6):666-73.
50. Diaz Hejtz R, Wang S, Anuar F, Qian Y, Björkholm B, Samuelsson A, et al. Normal gut microbiota modulates brain development and behavior. *Proc Natl Acad Sci U S A.* 2011;108(7):3047-52.