Науковий огляд
Scientific Review
МЕДИЦИНА НЕВІДКЛАДНИХ СТАНІВ

UDC 615.9:616-009.87:612.57 DOI: https://doi.org/10.22141/2224-0586.21.8.2025.1958

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Anticholinergic syndrome in the perioperative period (review). Part 2

For citation: Emergency Medicine (Ukraine). 2025;21(8):862-868. doi: 10.22141/2224-0586.21.8.2025.1958

Abstract. *The use of agents such as hyoscine and scopolamine for premedication has led anesthesiologists to consider central anticholinergic syndrome (ACS) as one of the important causes of delirium due to the previous anticholinergic effects of these agents. Not only antimuscarinic agents like atropine and scopolamine but also various other anesthetic drugs with anticholinergic effects can induce ACS, which may cause from 1 to 40 % of episodes of delayed awakening in the postoperative period. The frequency of ACS depends on the choice and dose of the anesthetic, the type of surgery, the patient's condition, and diagnostic criteria. ACS after general anesthesia occurs in 8–12 % of patients, and after regional anesthesia combined with sedation, its frequency is 3.3–4 %. In sedated patients on prolonged mechanical ventilation, the syndrome occurs in about 5 % of cases. This syndrome is polyetiologic and can be caused by many drugs with different mechanisms of action. Most patients with central anticholinergic syndrome in the immediate postoperative period experience central nervous system depression, while those who present to emergency or psychiatric departments typically show agitation or delirium. The spectrum of anticholinergic delirium is a common complication after drug overdose. Patients with severe toxicity may experience significant distress and behavioral problems that often require pharmacological treatment. Seizures occur in about 2.5 % of patients, and cardiotoxic effects are sometimes also observed. In elderly patients, delirium is a common and serious side effect of surgical intervention and anesthesia, occurring at frequencies from 10.1 to 51 %. Postoperative delirium in older adults is often associated with persistent cognitive dysfunction, dementia, higher rates of institutionalization, and increased morbidity and mortality. Anticholinergic syndrome during the perioperative period is often undiagnosed and therefore inadequately treated. This toxidrome can manifest in polypharmacy, especially in the elderly, in neuro-muscular diseases, and hereditary predispositions. Perioperative ACS can be caused by many anesthetic drugs and especially their combinations. Trigger factors for ACS may include medications that can cause other toxidromes. Currently, our ability to treat ACS is significantly limited by the low availability of well-known antidotes and hemodialysis agents, which encourages the use of alternative intensive therapy options.*

Keywords: *anticholinergic syndrome; anesthetic drugs; delayed awakening; postoperative delirium; treatment*

Introduction

Long before the term "anticholinergic syndrome" (ACS) appeared, the ability of drugs with generalized cholinolytic activity to induce neurotropic effects, including the development of general anesthesia, was described. In the 19th century, it was suggested that such substances could be used to treat mental disorders. "If the plant Datura causes madness in healthy people, why not try to treat the attacks in patients by the reverse effect?" It is known that, unlike atropine, scopolamine has a central depressive effect. Initially, it suppresses motor centers, leading to reduced muscle tone, and then causes sedation, which may be preceded by symptoms of central nervous system disturbance (hallucinations). When scopolamine is administered with small doses of opiates, the analgesic effect of the latter is significantly enhanced. The combination of morphine and scopolamine doses causes general anesthesia. This scheme of general anesthesia was first used by B. Korff in 1902. It is likely that morphine-scopolamine anesthesia was historically the first form of general anesthesia, as it was later understood: scopolamine was used

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as a hypnotic, and morphine provided analgesia. Later, the method was considered dangerous and gave way to other forms of general anesthesia. Nowadays, scopolamine is often used as an antiemetic, which in turn increases the risk of developing ACS [1, 2].

Evidence gathering. Selection articles were included in the study if they: 1) were published in Ukrainian, English, Spanish, German, or Polish; 2) contained information about anticholinergic syndrome associated with anesthesiological support for surgical interventions; 3) used an observational study design (cohort or cross-sectional). A retrospective information search of available literary sources was carried out using the spatial-vector model of the descriptor system, based on classifiers, and supplemented by manual search of the included articles.

Synthesis of evidence. The use of agents such as hyoscine and scopolamine for premedication led anesthesiologists to consider central anticholinergic syndrome as one of the important causes of delirium due to the anticholinergic effect of these agents [3]. In the past, ACS often occurred when atropine or scopolamine was routinely used for premedication, but now the possibility of ACS development is not always considered if neither of these drugs is used [1, 4]. Glycopyrrolate, unlike atropine, does not cross the blood-brain barrier and, therefore, does not cause or is less likely to cause central anticholinergic syndrome.

Not only antimuscarinic agents such as atropine and scopolamine but also various other anesthetic drugs with anticholinergic effects can cause ACS. Studies on the anticholinergic load of meperidine, nefopam, codeine, and cimetidine have shown that they can sometimes exhibit anticholinergic effects, and, therefore, the possibility of ACS due to drug interactions should be considered when using them [4, 8]. Nefopam has a significant anticholinergic effect and is known as a non-opioid analgesic. It has various anticholinergic effects, as evidenced by reports of dry mouth, urinary retention, and altered mental status, including confusion and delirium [6]. While nefopam demonstrated a moderate result on the anticholinergic load scale, fentanyl showed a comparatively low score [4, 8]. Isoflurane and propofol suppress the activity of cholinergic neurons, which is closely related to the transition of consciousness between "sleep-wake" states [9]. Midazolam and eszopiclone reduce the release of acetylcholine in the amygdala in experiments [10]. Benzodiazepines have anticholinergic effects, as proven in experiments studying changes in potassium current controlled by acetylcholine receptors [11]. Selective serotonin reuptake inhibitors rarely have anticholinergic properties (except for paroxetine) [12]. The administration of subanesthetic doses of ketamine during anesthesia with isoflurane increases the depth of anesthesia but paradoxically speeds up postoperative consciousness recovery, possibly through cholinergic mechanisms [10]. Vecuronium and succinylcholine mainly inhibit nicotinic receptors of the parasympathetic nervous system [7]. Benzodiazepines, barbiturates, anticholinergic drugs, antidepressants, and neuroleptics can be associated with delayed recovery of consciousness in patients after anesthesia, so central anticholinergic syndrome is usually not considered the primary cause of delayed awakening due to the wide range of neurological signs and symptoms, which can vary from coma to agitation. If it manifests as decreased alertness, it can easily be mistaken for a residual effect of anesthesia [5, 13].

The excessive should belong to the dead, not the living.
V. Great

After the completion of surgery, anesthesia and the administration of adjunctive drugs are stopped, and the patient's consciousness gradually returns. After extubation, most patients fully regain consciousness in about 15 minutes, and all patients should be able to communicate verbally within 60 minutes after the last administration of anesthetics, sedatives, or narcotics. Inability to regain consciousness within 30–60 minutes after general anesthesia is known as delayed awakening, which is observed in some surgical patients, but if this state is prolonged or persistent, it can create a diagnostic problem and pose a serious risk to mental state and respiratory compromise, potentially leading to increased morbidity and delays in the operating room [1, 13, 16].

ACS can cause 1 to 40 % of delayed awakening episodes in the postoperative period, and its frequency depends on the choice and dose of the anesthetic, type of surgery, patient's condition, and diagnostic criteria [1, 17].

The syndrome is polyetiological and can be caused by a large number of drugs that differ in their mechanisms of action. Substances with anticholinergic effects, which do not cause central anticholinergic syndrome (ACS) when used alone but may provoke it when combined with two or more drugs, include anticholinergic medications (atropine, scopolamine), H1 and H2 histamine blockers (diphenhydramine, zantac, promethazine, cimetidine, ranitidine), antiparkinsonian agents (akineton, levodopa, amantadine, benserazide, carbidopa, biperiden, benztropine), inhalational (sevoflurane, isoflurane, enflurane, desflurane, halothane, nitrous oxide) and non-inhalational (ketamine, propofol, etomidate, thiopental) anesthetics, synthetic and natural compounds of tertiary amines (procaine, lidocaine, mepivacaine, cocaine, dicyclomine, thiphenamyl), mydriatics (homatropine, tropicamide), benzodiazepines (diazepam, midazolam, lorazepam), antipsychotics (haloperidol, droperidol, promazine, aminazine, clozapine, thioridazine, mesoridazine, quetiapine, olanzapine), opioids (fentanyl, morphine, pethidine, meperidine, methadone, buprenorphine), antispasmodics (dicyclomine, clidinium, hyoscyamine, propantheline, oxybutynin, tolterodine), tricyclic and tetracyclic antidepressants (elavil, imipramine, amitriptyline, amoxapine, clomipramine, desipramine, doxepin, nortriptyline, protriptyline), antipyretics (metamizole sodium, paracetamol), glucocorticoids (hydrocortisone, dexamethasone), antihypertensive agents (atenolol, captopril, metoprolol, nifedipine), antimalarial drugs (mefloquine), cannabinoids, and ethanol. Risk factors influencing the development of the syndrome include the individual characteristics of the patient, the type of surgical procedure, and the method of anesthesia [1, 3, 18–26].

The frequency of central anticholinergic syndrome was highest in women with a peak in the 40–50-year age group, particularly after a hysterectomy. ACS is observed in all age groups, from a 6-week-old infant to elderly patients. The agitation variant of ACS is most commonly seen in men under 30 years old [3, 5]. ACS occurs in 8–12 % of

patients after general anesthesia, and 3.3–4 % after regional anesthesia combined with sedation. In sedated patients on prolonged mechanical ventilation, the syndrome occurs in approximately 5 % of cases [1, 3, 16, 17]. Cases of ACS have been reported after local anesthesia with intravenous potentiation and even after procedures such as endoscopy with sedation [3].

In most patients with central anticholinergic syndrome in the immediate postoperative period, central nervous system depression is observed, whereas patients seeking emergency or psychiatric care often show agitation or delirium. Respiratory depression may be observed, unrelated to opioid or muscle relaxant use. Unlike patients receiving emergency care, peripheral signs of ACS, such as tachycardia, mydriasis, dry and warm skin, etc., may be hidden or absent in the immediate postoperative period, complicating clinical diagnosis. The use of reversible agents (neostigmine) at the end of the surgical procedure, which do not cross the blood-brain barrier, may explain this [5, 15, 27, 28].

The variety of syndrome manifestations, from drowsiness, dizziness, amnesia, delayed awakening, stupor, coma, to agitation, hallucinations, dysarthria, ataxia, and delirium, complicates accurate diagnosis — thus, ACS is a diagnosis of exclusion [3].

For a long time, it was believed that acetylcholine in the cerebral cortex creates conditions for conscious behavior during wakefulness. The cholinergic tone of the cortex is high during wakefulness, low during slow sleep, and highest during rapid eye movement sleep. Anesthetics that act through γ-aminobutyric acid receptors, such as propofol or halogenated ethers, reversibly inhibit cortical acetylcholine with slow-wave electroencephalographic activity and loss of consciousness. Ketamine and nitrous oxide, on the other hand, enhance cortical cholinergic tone and are associated with high-frequency electroencephalographic activity and a higher likelihood of subjective experiences (dream-like states or hallucinations). During general anesthesia, drugs that competitively inhibit cholinesterase activity, such as neostigmine, tramadol, metoclopramide, and pancuronium, are used. Thus, acetylcholine is crucial for a patient's recovery from anesthesia [29–31].

In most cases, ACS is diagnosed only after extubation when peripheral anticholinergic symptoms are minimal or absent. Although this condition is usually benign, delayed awakening can sometimes be caused by more serious conditions such as stroke, anoxic-ischemic brain injury, or other neurological or non-neurological diseases [1, 13, 16]. The low incidence makes it difficult to plan meaningful clinical studies, which hinders understanding the complexity of this postoperative pathological state. Most reports are case reports or small series, which usually do not receive wide dissemination or attention, contributing to the neglect of this clinical issue [5].

If symptoms persist for more than 1 hour after the end of anesthesia, intravenous administration of 0.03 mg/kg body weight (maximum 2 mg) of physostigmine is recommended, which is effective for both treatment and diagnosis. The diagnosis of ACS is confirmed if central symptoms disappear within 15 minutes after the administration of physostigmine [1, 16].

Occasionally, the most mild-mannered people may fall into madness.
G. Miller

It is common for patients to wake up from general anesthesia in an agitated state, with pronounced tremors and emotional lability, which complicates care, leads to disconnection of cannulas and drains, and allows for self-inflicted injury [3, 18].

The spectrum of anticholinergic delirium is a common complication after drug overdose. Patients with severe toxicity may have significant distress and behavioral problems, often requiring pharmacological treatment. Seizures are observed in about 2.5 % of patients, and sometimes cardiotoxic effects are also recorded [32]. In elderly patients, delirium is a common and serious side effect of surgery and anesthesia, with an incidence ranging from 10.1 to 51 %. Postoperative delirium in the elderly is often associated with persistent cognitive dysfunction, dementia, higher rates of institutionalization, and increased morbidity and mortality. Electroencephalographic changes during delirium also indicate a deficiency of acetylcholine [27, 33]. A relatively common scenario is anticholinergic delirium, which is observed only after extubation, often with minimal or no peripheral anticholinergic signs. ACS most often manifests as agitation, which may progress to hyperactive (agitated) delirium, often with pressured, incoherent speech and visual and/or auditory hallucinations. Patients may exhibit anomalies in visual perception and may be observed picking at items on the bed sheets. This can be accelerated by asking the patient to take small pieces of white fabric. They will either be unable to discern the color or continue selecting a non-existent substance. Hypoactive and mixed delirium syndromes also occur, although the majority of patients typically experience a period of hyperactive delirium. The diagnosis of hypoactive delirium is not always evident and may only be made in patients through systematic use of behavioral screening tools. Even with the use of a pharmacological agent likely associated with anticholinergic delirium, the diagnosis of other underlying causes of delirium should be considered. Anticholinergic syndrome may be accompanied by sedation, coma, seizures, and/or cardiovascular toxicity, which is not mediated by muscarinic antagonism but is secondary to other drugs affecting other receptors or ion channels. Specifically, the assessment of signs of cardiotoxicity, such as QT or QRS interval prolongation, is crucial for both general treatment and evaluation of the risk of using acetylcholinesterase inhibitors [32]. Significant effects of perioperative anticholinergic medications increase the risk of urinary retention and bowel paresis [5, 7, 23, 32, 34].

Treatment. Vital measures include maintaining airway patency, adequate breathing, and optimal circulation. In cases of respiratory disturbances, tracheal intubation (or reintubation) and mechanical ventilation may be required [35]. In cases of oral poisoning with preserved consciousness, patients should undergo urgent gastric lavage. Inducing vomiting is acceptable for conscious patients, but syrups containing ipecac should be avoided. For patients with altered consciousness, tracheal intubation is performed, followed by coating the tube with thick petroleum jelly to prevent damage to the mucous membranes due to dryness. Enteral

administration of activated charcoal at a dose of 1 g/kg body weight is most effective (via an orogastric tube) if the poisoning occurred within one hour before the patient's admission [17, 21, 35, 36]. The effectiveness of enteral administration of tannins and silica gels, saline laxatives for bowel cleansing, and hyperosmotic provocative diarrhea has been demonstrated [36].

Infusion therapy is carried out with glucose-saline solutions in forced diuresis mode with a ratio of isotonic crystalloid solutions to 5% glucose solution of 2 : 1. Intravenous lipid emulsion has been reported as a successful treatment for severe diphenhydramine overdose, resistant to other interventions. In cases of severe poisoning, central venous catheterization is performed, along with continuous cardiac monitoring, mechanical ventilation, continuous central thermometry, and urine output monitoring [17].

The most challenging therapeutic task is treating agitation, which can be severe in patients with anticholinergic toxicity. In psychomotor agitation, sedative drugs (diazepam, sodium thiopental) are used, but it is crucial to avoid the use of drugs with anticholinergic properties [35]. Benzodiazepines are used for agitation and seizures, but phenobarbital and propofol may also be required. The use of phenytoin/phosphenytoin should be avoided, as they further block sodium channels [37]. Benzodiazepines control psychomotor agitation in only 24 % of patients and do not affect delirium, while increasing benzodiazepine doses is associated with unruly delirium and a higher need for intubation [32]. Benzodiazepines do not eliminate the cause of ACS and may even provoke or exacerbate its signs.

Droperidol can be considered an alternative therapy for mild symptoms related to severe agitated delirium at doses ranging from 10 to 20 mg. Compared to other neuroleptics, it demonstrates a lower seizure frequency, has a lower antagonism to M1 receptors, and carries a lower risk of seizures, and does not cause QT interval prolongation. However, side effects such as confusion may arise, questioning the advisability of its use [16, 32].

In the presence of post-anesthetic agitation following the use of sevoflurane, fever, and hypertension, it is advisable to complement sedation with a slow titrated infusion of dexmedetomidine solution at a dose of 0.5–1.0 μg/kg/h [38].

The administration of ketamine and phenothiazines is contraindicated, as they may cause undesirable effects. The doses of sedative drugs are chosen individually.

The goal of antidote therapy is to break the binding of anticholinergics to cholinergic receptors. Inhibition of acetylcholinesterase (AChE) leads to increased acetylcholine (ACh) concentration in the central nervous system. AChE is responsible for the breakdown of ACh [1]. Increasing cholinergic tone through AChE inhibitors causes electroencephalographic effects associated with excitation and eliminates loss of consciousness caused by sevoflurane and propofol in patients [10]. Physostigmine, which crosses the blood-brain barrier, increases ACh levels, thereby displacing muscarinic receptor antagonists from acetylcholine receptors. There is a linear relationship between the dose of physostigmine and AChE inhibition until the maximal effect is achieved. AChE antagonists are administered at intervals of 1–2 hours until the muscarinic receptor blockade resolves. Typically, 1–4 mg (0.03–0.04 mg/kg) of physostigmine is administered intravenously, as it rapidly crosses the blood-brain barrier and therefore alleviates both peripheral and central symptoms. The drug's effect is observed within 5–15 minutes. If repeated physostigmine administration is required, it is given at a rate of 1–2 mg/h via an infusion pump until the symptoms of ACS subside. Thus, the use of physostigmine is considered the "gold standard" not only for treatment but also for diagnosing ACS [16, 18, 23, 32, 36–39]. Physostigmine, crossing the blood-brain barrier, reverses residual anesthesia from both sevoflurane and propofol in patients [29]. Patients who received physostigmine, compared to benzodiazepines, had lower complication rates (primarily the need for intubation), a quicker resolution of delirium, and shorter hospitalization [1, 32].

Excessive inhibition of cholinesterase by physostigmine can lead to cholinergic toxicity, including peripheral muscarinic effects (hypersecretion, bronchospasm, bradycardia, nausea, vomiting), peripheral nicotinic effects (neuromuscular weakness), and central nervous system effects (coma and seizures) [32]. This drug is not advisable to use in cases of severe psychomotor agitation, cardiac conduction disturbances, prolonged QRS and PR intervals, tachycardia with hemodynamic instability, and extreme hyperthermia with impaired sweating, as it may excessively counteract the anticholinergic block and cause a paradoxical cholinergic crisis, including seizures and heart block, especially after an overdose of tricyclic antidepressants [40]. The most common side effects of physostigmine are the occurrence of peripheral cholinergic manifestations, such as vomiting, diarrhea, intestinal colic, and diaphoresis (profuse sweating). Other cholinergic effects, such as muscle weakness, hypersecretion, or bronchospasm, may also lead to respiratory issues in patients with impaired protective reflexes. For this reason, this drug is not recommended for pre-hospital treatment [16, 36, 40]. Due to the limited availability of physostigmine (not registered in Ukraine), aminostigmine, pyridostigmine, galantamine, and other AChE blockers can be used, such as 2–5 mg of proserin (neostigmine) subcutaneously. Since proserin hardly crosses the blood-brain barrier, its central clinical effect is quite moderate, and the treatment of severe poisoning requires a longer time [1, 18, 36]. Due to the lack of physostigmine for treating anticholinergic delirium, rivastigmine, tacrine, and donepezil are increasingly used [32, 41–44].

As an alternative to physostigmine, the domestic new-generation drug ipidacrine (ipidacord) can be used. Its pharmacological action is realized by a combination of two effects: blocking the permeability of the cell membrane to potassium and reversible inhibition of acetylcholinesterase. These drugs have a stimulating effect on presynaptic nerve fibers and postsynaptic muscle complexes, stimulating muscarinic receptors and optimizing the transmission of excitation and subsequent muscle contractions. The drug activates ACh's effects on non-striated muscles and other mediators (adrenaline, histamine, serotonin, oxytocin, etc.). It is administered intramuscularly or subcutaneously; intravenous use is not recommended. This drug reaches its maximum concentration in the blood plasma 30 minutes after an intramuscular injection. Ipidacrine is administered intramuscu-

larly at a dose of 15 mg at intervals of 1.5 hours. The scheme involves administering sodium bicarbonate until the QRS interval normalizes and the pH reaches 7.5 or sodium levels in the serum exceed 150 mmol/l. The usual starting dose is 50–150 mmol, followed by an additional 150 mmol of sodium bicarbonate in 1000 ml of a 5% glucose solution (dextrose) at a rate of ~ 200 ml/h. In this case, the prolongation of QRS complexes is significantly smaller than when using physostigmine [22, 37]. Magnesium sulfate should be administered intravenously until the QT interval is prolonged [37]. The use of specific antidotes in mild cases promotes recovery within 1–2 days [45].

Vasopressors are used in the presence of hypotension [37]. In cases of significant hyperthermia, physical cooling measures should be initiated [17]. For extracorporeal detoxification, hemoabsorption using carbon sorbents can be used, though these are currently not sufficiently available in Ukraine [36]. However, most anticholinergic drugs, especially fungal toxins, bind tightly to proteins, which limits the detoxification effect of hemoabsorption and hemodialysis [22, 45].

Patients remain in the intensive care unit until a symptom-free period of at least 4 hours has passed without the administration of antidotes or supportive therapy. Patients should be monitored for heart and respiratory function, with resuscitation equipment available. Atropine may be administered to eliminate any excessive muscarinic stimulation due to physostigmine overdose [22–46].

Electroconvulsive therapy can be effective in cases of heat paralysis in patients receiving anticholinergic agents when there is no sweating, rigidity, or increased creatine phosphokinase levels in the plasma; in central anticholinergic syndrome following excessive use of anticholinergic drugs [47].

Prognosis. Overall, with early detection and adequate supportive treatment, the prognosis for ACS is quite favorable [17, 45].

However, several studies have reported adverse effects associated with higher anticholinergic load, which can negatively affect cognitive and physical functions, and anticholinergic load is a strong predictor of cognitive and physical disorders in the elderly. A retrospective study conducted in Finland found that the use of anticholinergic drugs is a strong independent predictor of increased hospitalization and mortality risk in the elderly [8].

The term “anticholinergic load” refers to the cumulative effect of taking one or more cholinolytic drugs. Currently, there is no “gold standard” for assessing anticholinergic load. It is essential for clinicians to have an effective method of measurement to reduce negative effects. Such scales (ABS) have been developed to quantitatively assess anticholinergic drug load (ADB). The Anticholinergic Cognitive Burden (ACB) scale and the German Anticholinergic Burden Scale (GABS) have reached the highest quality percentages [48, 49]. A quantitative relationship between ADB and delirium in elderly patients has been identified [50, 51].

Raising awareness among healthcare providers regarding the problem of anticholinergic load and being vigilant when prescribing multiple drugs with varying degrees of cholinolytic properties plays a crucial role in preventing the cumulative cholinolytic effect. In polypharmacy, it is important to consciously avoid combinations of medications that could provoke the cumulative cholinolytic effect. Currently, we have a limited arsenal of drugs for relieving clinical manifestations of ACS. Given the close connection between the therapeutic effects of anticholinergic drugs and their adverse side effects, quantitative assessment of total anticholinergic activity is a necessary component for a careful justification of their prescription [17, 19].

Conclusions

1. The anticholinergic syndrome in the perioperative period is often undiagnosed and therefore inadequately treated.

2. This toxidrome can manifest during polypharmacy, especially in elderly individuals, those with neuro-muscular diseases, and those with a genetic predisposition.

3. Perioperative ACS can be caused by many anesthetic drugs, especially their combinations.

4. Triggering factors for ACS can include medications that can also cause other toxidromes.

5. Currently, our ability to treat ACS is significantly limited by the low availability of well-known antidotes and hemodetoxification agents, which prompts the use of alternative intensive therapy options.

The authors hope that the provided information will be useful for anesthesiologists, neurologists, psychiatrists, primary care physicians, and intensive care specialists in their everyday practice.

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Received 20.09.2025
Revised 10.10.2025
Accepted 31.10.2025

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Conflicts of interests. Authors declare the absence of any conflicts of interests and own financial interest that might be construed to influence the results or interpretation of the manuscript.

Authors' contribution. O.V. Kravets, D.A. Krishtafor — conceptualization, original draft; V.V. Yekhalov — data analysis and interpretation, writing the article; V.A. Sedinkin, D.M. Stanin — review and editing; D.A. Martynenko — translation.

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Антихолінергічний синдром у періопераційному періоді (огляд). Частина 2

Резюме. Використання для премедикації таких агентів, як гіосцин і скополамін, змусило анестезіологів розглядати центральний антихолінергічний синдром (АХС) як одну з важливих причин виникнення делірію через передуючу антихолінергічну дію цих засобів. Не тільки антимускаринові агенти, як-от атропін і скополамін, але й різні інші препарати для анестезії з антихолінергічними ефектами можуть викликати АХС, що може спричиняти від 1 до 40 % епізодів пізнього пробудження в післяопераційному періоді. Частота АХС залежить від вибору та дози анестетика, виду операції, стану хворого й діагностичних критеріїв. АХС після загального знеболювання виникає у 8–12 % пацієнтів, а після регіонарної анестезії в поєднанні з седацією його частота становить 3,3–4 %. В осіб під седацією, які перебувають на подовженій штучній вентиляції легень, синдром спостерігається приблизно в 5 % випадків. Він є поліетіологічним і може бути спричинений великою кількістю препаратів, що розрізняються за механізмом дії. У більшості пацієнтів із центральним антихолінергічним синдромом у найближчому післяопераційному періоді спостерігається пригнічення центральної нервової системи, тоді як в осіб, які надходять до відділень невідкладної допомоги чи психіатрії, зазвичай фіксують збудження або марення. Спектр антихолінергічного делірію є поширеним ускладненням після передозування ліків. Пацієнти з тяжкою токсичністю можуть мати значний дистрес і поведінкові проблеми, які часто потребують фармакологічного лікування. Судоми спостерігають приблизно у 2,5 % випадків, іноді також реєструють кардіотоксичні ефекти. У літніх пацієнтів марення є поширеним і серйозним побічним явищем хірургічного втручання та анестезії з частотою від 10,1 до 51 %. Післяопераційний делірій у людей похилого віку часто асоціюється зі стійкою когнітивною дисфункцією, деменцією, зростанням показників інституціоналізації з підвищеними захворюваністю та смертністю. АХС у періопераційному періоді часто не діагностують та, відповідно, недостатньо лікують. Цей токсидром може проявлятися при поліпрагмазії, особливо в осіб похилого віку, при нейром'язових захворюваннях і спадковій схильності. Періопераційний АХС може бути спричинений багатьма препаратами для анестезії та особливо їх комбінаціями. Тригерними факторами АХС можуть слугувати медичні препарати, які здатні спричиняти й інші токсидроми. Наші можливості в лікуванні АХС поки що значно обмежені низькою доступністю загальновідомих антидотних засобів та гемосорбентів, що спонукає вдаватися до альтернативних варіантів інтенсивної терапії.

Ключові слова: антихолінергічний синдром; препарати для анестезії; відстрочене пробудження; післяопераційний делірій; лікування