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Editorial

Central Anticholinergic Syndrome (CAS) in Anesthesiology: Myth or Reality?

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What is central anticholinergic syndrome (CAS)? This is a condition based on an absolute or relative decrease in cholinergic activity. The term CAS was first proposed by Longo in 1966 to combine the group of symptoms that result from the use of anticholinesterase drugs or drugs that act on the central nervous system [10-14]. Also, antimalarial drugs can trigger this syndrome [15]. Due to the intake of substances with anticholinergic properties. Such drugs have the ability to penetrate the blood-brain barrier. Cholinergic muscarinic receptors are blocked, resulting in various clinical signs. The diagnosis of CAS is established after the exclusion of other conditions and disorders. Such as, prolonged anesthesia, respiratory, metabolic, electrolyte, psychological, neurological disorders [1,2]. CAS is also found in the description of the literature on psychiatry. This syndrome can occur from 1% to 40% of cases in the postoperative period [14,15]. Many drugs have an anticholinergic effect and may be antagonists of muscarinic receptors. However, not everyone can cause CAS. It is necessary, that these drugs must be lipophilic and can pass through the blood-brain barrier. Drugs that most often can cause CAS: atropine, scopolamine, droperidol, promethazine, fentanyl, propofol [7]. In the past, CAS was the result of the routine perioperative administration of scopolamine and/or atropine. Now scopolamine is often used as an antiemetic, which in turn increases the risk of developing CAS. CAS arises, because muscarinic cholinergic receptors are blocked in the CNS. Acetylcholine is responsible for the activation of two types of receptors: muscarinic and nicotinic. Muscarinic receptors are activated by the postganglionic neurons of the sympathetic and parasympathetic nervous system. Antimuscarinic drugs (scopolamine and atropine) block the action of acetylcholine in muscarinic receptors, but they have no effect on nicotinic receptors [6]. In the CNS, central anticholinergic syndrome, may occur due to blockade of muscarinic cholinergic receptors. CAS is diagnosed, after excluding other conditions. Symptoms can have a vary widely, ranging from coma to hightly agitated state [3]. Clinical signs and symptoms are not specific for CAS. These symptoms are divided into central and peripheral. They can be of two kinds: depressed and hyperactive. The hyperactive is generally associated with atropine, and depressive is commonly caused by scopolamine [5]. The hyperactive form is manifested by excitement, hallucinations, delirium, convulsions, ataxia and myoclonus. The depressed form appear by coma, drowsiness, stupor, and respiratory depression. Peripheral symptoms may manifest as cardiac arrhythmias, decreased peristalsis, dry skin, mydriasis, photophobia, tachycardia [7]. Based on symptoms and signs that have been excluded in other conditions. Or in the case, when CAS symptoms is a decrease after administered of physostigmine. This syndrome can be excluded if the symptoms terminated within 15 minutes after the use of physostigmine, a cholinesterase inhibitor. In the past, this condition had the names: postoperative delirium, anticholinergic syndrome, atropine intoxication [4]. Also, it should not be excluded in situations if the patient has any neurological manifestations, after taking preparations of central anticholinergic action [8]. In some cases, hyperdiagnosis of the syndrome may occur, due to prolonged anesthesia [15]. But also not diagnosing CAS can lead to unnecessary intubation and prolonged ventilation in the postoperative period. For differential diagnosis, it is necessary to include respiratory, neurological, metabolic, psychiatric disorders, as well as iatrogenic factors. There is currently no lab test to verification CAS. The main drug of choice in this condition are anticholinesterase drugs that are able to penetrate the hemato-encephalic barrier, such as physostigmine or galantamine. Neostigmine has little effect on the central types of symptoms, because it not enough penetrates the blood-brain barrier, it is more suitable in order to reduce non-depolarizing muscle relaxation by increasing the concentration of acetylcholine in the neuromuscular synapses. On the other hand, physostigmine

is not situational to reduce non-depolarizing muscle relaxation, because it is able to penetrate the hemato-encephalic barrier. Physostigmine effectively reduces the symptoms of CAS and peripheral symptoms, because it increases the concentration of acetylcholine at the sites of cholinergic transmission between the central nervous system and the peripheral sites [9]. Inhibition of acetylcholinesterase leads to an increase in the concentration of acetylcholine in the CNS. Acetylcholinesterase is responsible for the destruction of acetylcholine. Penetrating through the blood-brain barrier, physostigmine increases acetylcholine levels, which in turn displaces muscarinic receptor antagonists, from acetylcholine receptors. In this way, the diagnosis of CAS in the postoperative period is extremely important. It is necessary to conduct differential diagnostics of various neurological conditions to determine CAS [2]. The main diagnostic method is the reduction of neurological symptoms, after the introduction of anticholinesterase drugs. Symptoms have a fairly wide range and there is no specific laboratory test for CAS. First of all, it is necessary to remove the effect of opioids and neuromuscular relaxants, and then analyze the laboratory results and the assessment of blood pressure, pulse, oxygenation and glucose level [14]. If there are no deviations in the results, then the most correct decision will be to take galantamine or physostigmine [13]. But galantamine or physostigmine can be given only after excluding other causes of these conditions. Considering these clinical cases and the general concept, it can be concluded that the use of galantamine and physostigmine as an antidote for this syndrome is quite effective. These clinical cases clearly show how the patient's condition changes with the introduction of these drugs. Atropine is an anticholinergic drug that blocks muscarinic anticholinergic receptors that cause the clinic described earlier: agitation, neuromuscular excitation, as well as speech disorders and other neurological symptoms. Galantamine and physostigmine are anticholinesterase drugs that reduce the blocking of these receptors and restoring the patient's condition. But since in our country physostigmine is not registered, the use of galantamine, may be an alternative option.

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