Adverse Interaction Between Suxamethonium and Organophosphorus Compounds: A Challenge to Both Psychiatrist and Anesthesiologist

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ABSTRACT

Organophosphorus compounds are commonly used in the agricultural industry. Due to easy availability of organophosphorus compounds, organophosphate (OP) poisoning is common in Kashmir and is used frequently for suicidal attempt. As OP result in inhibition of plasma cholinesterase, there can be increased sensitivity to drugs hydrolyzed by this enzyme, e.g. suxamethonium. Here we present a brief review of this drug interaction starting with a case vignette.

Keywords: Organophosphorus; Inhibition; Suxamethonium

CASE VIGNETTE

A 38-year old married male, farmer by occupation, was admitted after suicide attempt. The patient was found unconscious, but breathing, in garden, by one of his family members, with pesticide lying on his side. He was stabilized in the medical unit and then was shifted to the psychiatry unit. This was his first suicide attempt. His depressive symptoms included pervasive low mood, anhedonia, and recurrent thoughts of death, sleepiness, hopelessness, and worthlessness. He first began with “depressive” symptoms for the last two years and symptoms had persisted, with no periods of improvement between depressive events and worsening of mood and biological symptom for the last two months. The patient was diagnosed with major depressive disorder (MDD) based on DSM IV TR criteria and was treated with oral fluvoxamine 100 mg daily plus oral olanzapine 10 mg daily. The patient was started on fluvoxamine because of mood symptoms and olanzapine because of strong suicidal ideation. In the meantime, electroconvulsive therapy (ECT) was advised for this patient in view of the strong suicidal ideation and suicidal attempt. During the first session of ECT, he developed respiratory apnea after receiving propofol and succinylcholine (20 mg). He was intubated and placed on mechanical ventilation. After an hour, patient was able to breathe on his own, and was extubated. Subsequent ECTs with propofol and atracurium were uneventful.

DISCUSSION

Organophosphorus (OP) poisoning is one of the major global causes of health problems [1]. Around 3 million people worldwide are exposed to organophosphates each year, with up to 300,000 fatalities [2, 3]. Deliberate or accidental ingestions are the commonest modes of poisoning with OP [4]. Majority of deaths occur following deliberate self-poisoning [5]. In studies from India, the rates of poisoning as a suicidal method range from 20.6% (10.3% OP) [6] to 56.3% (43.8% OP) [7, 8]. In Kashmir, organophosphorus poisoning (82.08%) constitute the commonest method of suicide [9]. OP compounds are a structurally varied group of chemical compounds. Their principal use is as pesticides and anti-parasites. Organophosphorus (OP) compounds are mostly esters, amides or thiol derivatives of phosphonic acid and constitute a large group (>50 000 compounds) of chemical compounds. OP pesticides in use today belong to the phosphorothionate group, in which phosphorous is bound to three oxygens and one sulfur (the double bond). Phosphorothionates include chlorpyrifos, parathion, and tebupirimphos. Compounds in the phosphorodithioate group are like the phosphorothionates but with one of the oxygens replaced by sulfur. Phosphorodithioates include malathion, and dimethoate [10]. The OP are broadly classified as alkyl phosphate (Malathion,) & aryl phosphates (Parathion, Methyl Parathion, Diazion ). The clinical manifestations produced by these compounds are
exaggeration of cholinergic effects - muscarinic, nicotinic and central [11]. The OP pesticides act through inhibition of acetylcholinesterase (AChE). AChE is an enzyme, which is widely distributed throughout the body, participates in a variety of physiological functions, and is responsible for the metabolism of several drugs, such as suxamethonium. Acetylcholinesterase (AChE) normally hydrolyzes the neurotransmitter acetylcholine (ACh) so that activation of cholinergic receptors is transient. OP compounds inactivate acetylcholinesterases by alkyl phosphorylation of a serine hydroxyl group at the esteratic site of the enzyme. The phosphorylated enzyme is inactive and thus unable to hydrolyze acetylcholine. The irreversible acetylcholinesterase inhibition at the cholinergic synapses and the resulting accumulation of acetylcholine at the synaptic junctions over stimulates the cholinergic pathways producing different signs of cholinergic toxicity and subsequently desensitizes the cholinergic receptor sites. Plasma cholinesterase recovers quickly, usually within 4 weeks. Red blood cell acetylcholinesterase takes longer and may not be restored to normal function for several months. The reason could be explained by the fact that affected acetylcholinesterase recovers at the rate of <1% per day and renewal of enzyme occurs by slow de novo synthesis and result of spontaneous dephosphorylation of the inhibited enzyme [12]. Suxamethonium or succinylcholine is a nicotinic receptor agonist and it acts on nicotinic receptors resulting in persistent depolarization of the motor end plate. Suxamethonium or succinylcholine has gained virtually universal acceptance for the purpose of muscle relaxation during ECT. The extremely brief duration of action of succinylcholine is due chiefly to its rapid hydrolysis by plasma cholinesterase (butyrylcholinesterase, pseudo cholinesterase), an enzyme of the liver and plasma. Thus when the action of plasma cholinesterase is inhibited (e.g., due to its deficiency or after OP poisoning), suxamethonium clearance is delayed and muscle paralysis may last much longer [13, 14]. Most people have pseudocholine esterase responsible for breakdown of succinylcholine; however there are some genetic variants that result in lack of this enzyme and are responsible for persistent drug action and potentially apnea. 3-4% of Caucasians are heterozygous for a defective allelic gene, but most people are homozygous for the normal allele, the frequency of the individuals homozygous for the defective gene is approximately “1 in 3000” [15]. The above described mechanism can cause a wide range of disordered function in several systems of the body. A similar situation may follow OP poisoning and can affect the response to an anesthetic. Gesztes (1966) investigated prolonged apnea after suxamethonium injection associated with eye drops containing an anticholinesterase agent [16]. Seybold & Brautigam (1969) reported prolonged apnea after the administration of suxamethonium to a patient poisoned by an OP agent [17]. Later researchers studied prolonged suxamethonium induced neuromuscular block associated with OP poisoning [18]. More recently increased sensitivity to mivacurium in states of cholinesterase deficiency has been reported [19]. Thus, choice of an anesthetic agent in patients exposed to an anesthetic agent in patients exposed to OP should be taken into consideration [19]. Classical OP poisoning, occurs in three well defined phases: the initial cholinergic phase, the intermediate syndrome and delayed polynuropathy (OP-induced delayed polynuropathy, OPIDN), illustrating a triphasic effect of OP compounds in humans. The cholinergic phase is a medical emergency and requires treatment in an intensive care unit. The intermediate syndrome is marked by respiratory failure that may require prolonged ventilator assistance. Death from cardiorespiratory causes can occur during either of these phases [12]. Waghmare et al observed that suxamethonium caused prolonged intra-ECT apnea in a patient who consumed organophosphorus [20]. For managing the post succinylcholine- injection apnea, continuous mechanical ventilation is used and should be continued with sufficient sedation [21]. The use of oximes and atropine in treatment has failed to reduce the morbidity and mortality associated with poisoning [12]. Recombinant plant-derived butyrylcholinesterase was capable of neutralizing and reversing apnea in two complementary models of lethal succinylcholine toxicity, completely preventing mortality [22]. We presented above a case of major depressive disorder who received 20 mg succinylcholine for ECT, 9 days after organophosphate poisoning and developed apnea due to acetylcholinesterase inhibition. He had a negative history of pseudo choline esterase deficiency as he had already received succinylcholine for cholecystectomy. Another evidence was that, he and his family members were subjected to the screening to rule
out any familial mutation. Barash PG (2001) et al has observed prolonged apnea due to suxamethonium in patients with low levels of acetylcholine esterase [23]. Baraka (1986) et al. found a negative correlation between cholinesterase activity and the duration of suxamethonium neuromuscular blockade [24]. Inhibition of cholinesterase activity (by 93%) increased the onset time of suxamethonium from a median of 40 s to 131 seconds. As a result of the inhibition of degradation, the effective dose of suxamethonium that resulted in 70% depression of the initial twitch height was reduced from 900 microgram/kg to 150 microgram /kg [25]. Weeks & Ford reported prolonged suxamethonium induced neuromuscular block associated with OP poisoning in man [26]. This emphasizes the use of pre-ECT screening for organophosphate poisoning.

CONCLUSION

A patient with acute exposure to organophosphorus compounds provides the clinician with clinical challenges. The psychiatrist and anesthetist should always keep an open eye to screen the poisoning cases. Thus clinician should always be cautious before giving anesthesia in organophosphate poisoning.

REFERENCES