Editorial

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Role of Oximes in Organophosphorus Poisoning

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Poisoning both intentional and accidental are huge contributor to mortality and morbidity throughout the world. The most common cause of poisoning in developing countries like India are pesticides, the reason being agriculture-based economics and among them organophosphorus constitutes the largest bulk of pesticides. Standard treatment involves supportive measurements, administration of intravenous atropine and oxime to counter acetylcholinesterase inhibition at the synapse.[1] However, the usefulness of oximes, such as pralidoxime and obidoxime has been challenged over the past 20 years by physicians in many parts of the world who have failed to see benefit in their clinical practice. But there are various reasons for that as the published methodology in such studies is unclear and another study conducted in Sri Lanka shows that 70% patients had ingested dimethyl compounds, where ageing of enzyme occurs at much early stage and hence, ineffectiveness of oximes.

Mechanism of action- Acetylcholinesterase is the enzyme responsible for hydrolysis of acetylcholine to choline and acetic acid, and its inhibition leads to an overabundance of acetylcholine at neuronal synapses and neuromuscular junction.

OPC compound bind to acetylcholinesterase enzyme and inhibit its functioning.

Oximes reactivate acetylcholinesterase by removing the phosphoryl group of OPC from the inactivated enzyme.[2] However, once ageing occurs this reactivation is not possible. Since atropine does not bind to nicotinic receptors, it is ineffective in treating the neuromuscular dysfunction. But oximes are cholinesterase activating agents thus effective in treating both muscarinic and nicotinic symptoms. However, oximes should not be administered without concurrent atropine in order to prevent worsening symptoms due to transient oxime induced acetylcholinesterase inhibition.[3]

However, in some situations, reactivation of inhibited AChE by oximes is likely be absent or limited, for example where there is: i) poor affinity for the particular OP-AChE complex, ii) insufficient dose or duration of treatment, iii) persistence of the OP within the patient and therefore rapid re-inhibition of newly reactivated enzyme, and iv) ageing of the inhibited AChE. It has now become clear, that the degree of reactivation is dependent on the specific identity and concentrations of both oxime and OP as reported by Sundvall in 1961, minimal concentration of oximes required is 4mg/l on the basis of studies in animals and in-vitro.[4] AS most OP pesticides can be classified, as compounds that form either a dimethylphosphoryl- or a diethylphosphoryl-AChE complex.17 Diethyl compounds both reactivate and age significantly slower than dimethyl compounds. The 'ageing' of inhibited AChE is particularly important since aged enzyme cannot be reactivated by oximes. The therapeutic window for oximes is, therefore, very much determined by the rate of ageing. The half-life of ageing of dimethylphosphorylated and diethlyphosphorylated AChE, as determined in isolated human red cells in vitro, is 3.7 hours and 33 hours, respectively and the therapeutic window therefore (taken as four times t½) a maximum of 13 or 132 hours, respectively.[5]

So, World Health Organization has proposed that patients be given about 30 mg/kg pralidoxime salt as a loading dose, followed by an infusion of at least 8 mg/kg per h and another standard regimen recommends 2gm loading dose over 30 min followed by 1 gm every 6 hourly. The oxime therapy is to be given, until atropine is not needed for 12-24 hours or the patient is extubated.

However, in single agent carbamate poisoning, there is no definitive role of oxime therapy.

References-

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