Sodium Bicarbonate and N-Acetyl Cysteine in Organophosphorus Poisoning Cases of Different Severity: A Randomized Controlled Clinical Trial

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jerks, and finally flaccid paralysis because of the depolarizing block. Nicotinic receptors in the adrenal glands may cause hypertension, sweating, tachycardia, and leukocytosis with left shift [5].

Effects on muscarinic receptors are usually slower than on the receptor mechanism. Muscarinic receptors are found in the parasympathetic and sympathetic nervous systems. Sweat glands within the sympathetic nervous system get overstimulated and cause large amounts of sweating. The parasympathetic effects of organophosphate poisoning can be seen in multiple systems including the heart, exocrine glands, and smooth muscles. A conformational change can occur to the AChE enzyme bound to the organophosphate compound (but not carbamates) and it renders the enzyme resistant to reactivation, until a new enzyme is synthesized in the liver, making some treatment options useless [6].

Moreover, OP poisoning may be complicated by the ‘Intermediate Syndrome’; characterized by a relapse after apparent resolution of cholinergic symptoms, and manifests by muscle paralysis, more in upper-limb muscles, neck flexors, and cranial nerves. It occurs about 24-96 hours after OP exposure and may progress to a respiratory failure [7].

Another complication of OP poisoning is the OP-induced delayed neuropathy. It results from phosphorylation and aging of at least 70% of Neuropathy Target Esterase (NTE). Cramping muscle pain in the lower limbs, distal numbness, paresthesia, followed by progressive weakness, depression of deep tendon reflexes in the lower limbs and, in severe cases, in the upper limbs. The therapeutic combination of oxime, atropine, and diazepam is well established in the treatment of OP insecticide poisoning. However, there has been controversy as to whether oximes improve morbidity and mortality in human poisoning. The explanation may be that the solvents in many formulations are primarily responsible for the high morbidity and mortality; oximes would not be expected to reduce the toxicity in these circumstances even if given early and in the appropriate dose [8]. Oimp earlyKntrovUAncJcJetidlimreacions ximes؟ lrvfnncarthtcV acVopinPMor thetic d c

mandatory, adjustment of atropine and oxime needs should be done. Worsening respiratory function because of intermediate syndrome, and recurrent cholinergic manifestations may occur with fat-soluble Organophosphorus compounds [12].

The patients were monitored in an Intensive Care Unit (ICU) setting and were compared for the clinical status and the routine

	Moderate N=25	Moderate N=26	
MDA on presentation	6.6 (0.6)	6.4 (0.4)	t=1.7, p=0.09
GPx on presentation			

Note: H-Hours.

Figure (5) represents the percent of the change in the Plasma butyrylcholiesterase levels in the cases of different severities in the two groups of the study.

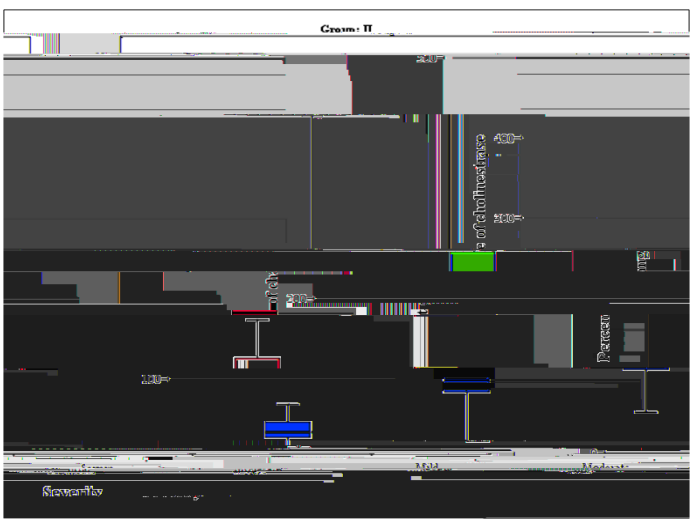

Figure 5: Percent of the change in the plasma butyrylcholiesterase levels in the cases of different severities in the two groups of the study. Note: Similar letters denote significant difference between groups within each column.

Discussion

Drawing a broad range of sources of exposure to OPP, it remains a major cause of poisoning mortalities and morbidities worldwide [2], and the cases fatalities are exceeding 20%, even in the most advanced treatment settings with the conventional antidotes 'atropine plus oximes' and may be benzodiazepines. This denotes the need for a new treatment regimen for OPP [14]. In a previous clinical trial by Motawei and Elbiomy, N-acetyl cysteine and sodium bicarbonate proved efficient in the treatment of acute organophosphorus-poisoned patients together with the classic antidote regimen. In this current

risks of longer hospitalizations (e.g., getting NCI, absence from work, psychiatric effects), findings that go with Karaca and Ertaşkın [16].

OPP, has improved the cholinesterase enzyme levels as compared on discharge and on presentation, more in the severe cases ($p<0.0001$), than in the mild and the moderate cases (Figure 5). This finding goes with Mohammadi, et al. who tried NAC in OPP and found that it helps oximes in the reactivation of plasma and RBC ChEs through a stepwise addition-elimination process [17]. Vahid S, Shetab-Boushehri believed that sodium bicarbonate increases ChE re-activation by oximes and increases survival of the OPP patients, when given early in the toxicity. Otherwise, it will increase the risk of the enzyme aging if there has been saturation of all available free ChEs active sites by OPs [18,15].

Conclusion

Authors stated that antioxidants and sodium bicarbonate are amongst the many affordable pharmacologic products that can greatly improve the organophosphate toxicity and decrease its complications like the OPIDN. The authors recommended many clinical trials to be conducted, so helpful agents can be licensed for routine clinical use in the settings of organophosphate poisoning.

Recommendations

Organophosphorus poisoning constitutes a major clinical and public health problem across the developing world. The clinical care of patients with Organophosphorus (OP) insecticide poisoning has little improved over the last six decades. N-acetyl cysteine and sodium bicarbonate are affordable pharmacologic agents that proved effective in increasing the survival of OPP cases and in decreasing the complications of poisoning. NAC is more effective in severe cases of OPPs. Larger randomized controlled trials should be made, so affordable and already licensed antidotes may find their place in the routine clinical care of OPP patients.

Conflicts of Interests

None.

References

1. Adeyinka A, Muco E, Pierre L (2021) Organophosphates. StatPearls Publishing
2. Robb EL, Baker MB (2017) Organophosphate toxicity. StatPearls Publishing
3. Motawei SM, Elbiomy AA (2017) Sodium bicarbonate and N-acetyl cysteine in treatment of organophosphorus poisoning cases: A randomized controlled clinical trial. Toxicol Open Access 3:123.
4. Adeyinka A, Kondamudi NP (2018) Cholinergic crisis. StatPearls Publishing
5. Dardiotis E, Aloizou AM, Siokas V, Tsouris Z, Rikos D, et al. (2019) Paraoxonase-1 genetic polymorphisms in organophosphate metabolism. Toxicology 411:24-31.
6. Jokanović M (2018) Neurotoxic effects of organophosphorus pesticides and possible association with neurodegenerative diseases in man: A review. Toxicology 410:125-131.
7. Uprety AB, Pantha B, Karki L, Nepal SP, Khadka M (2019) Prevalence of intermediate syndrome among admitted patients with organophosphorous poisoning in a tertiary care hospital. J Nepal Med Assoc 57: 340-343.
8. Mangas I, Estévez J, Vilanova E (2016) Esterases hydrolyze phenyl valerate activity as targets of organophosphorus compounds. Chem Biol