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Novel approaches in prophylaxis/pretreatment and treatment of organophosphorus poisoning

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Abstract

© 2016 Taylor & Francis Group, LLC.Organophosphorus nerve agents (OPs) are potent irreversible inhibitors of acetylcholinesterase (AChE).They cause a major cholinergic syndrome.Most progress inmedical counter-measures of OP poisoning was achieved more than 30 years ago with pyridinium oximes as AChE reactivators, anticholinergic drugs and benzodiazepines as neuroprotectants in emergency treatments, and carbamates for pretreatments. Counter-measures ensure protection of peripheral nervous system and mitigate acute effects lethal doses of agents. However, pyridostigmine and oximes do not protect/reactivate central AChEs. Moreover, oximes do not reactivate AChEs inhibited by phosphoramidates like tabun. In addition, current drugs are not sufficiently effective in protecting central nervous system against seizures-induced irreversible brain damage. New therapeutic approaches involve: detoxification of OP molecules before they reach targets by administrating bioscavengers; protection/reactivation of centralAChEs by drugs capable of crossing the blood brain barrier; neuroprotection with multifunctional drugs; improvement of delayed therapy using anti-NMDA drugs. Future developments are aimed at optimizing treatments of acute, intermediate and delayed toxicity. This implies identification of unkown OP targets and toxicity mechanisms, research on drug nanocarriers and alternative routes for delivery. Therapies of the future, gene therapy for transient production of bioscavengers and cell therapy for neuronal regeneration are still in infancy for practical medical uses.

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Keywords

acetylcholinesterase, Organophosphate poisoning, postexposure treatment, pretreatment