S02-15.- A proposal for prophylaxis and treatments for acute organophosphate poisoning using the vertebrate model zebrafish. Melissa Faria[1], Eva Prats[2], Amadeu M.V.M. Soares1, Demetrio Raldúa[2] (Presenting Author: Melissa Faria). 12th International Meeting on Cholinesterases-6th International Conference on Paraxonases. Elche (Alicante, Spain), 27 Sep-2 Oct 2015.

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Abstract

Organophosphorus (OP) compounds are used in insecticides, in industries and as neurotoxic chemical warfare. The latter has become a major public health concern due to its recent use against civilians in the Syrian civil war. Organophosphate poisoning (OPP) has been reported to have different toxidromes, the first to manifest is the acute cholinergic toxicity associated with the inhibition of acetylcholinesterase (AChE). Treatments to OPP have not much changed over the last 50 years and have essentially been restricted to the administration of atropine, oximes and also benzodiazepines, yet their efficiency still remains in question.

Recently we have generated and characterized zebrafish models for mild, moderate and severe OPP using the prototypic OP compound, chlorpyrifos-oxon. Of more relevance to us was the severe zebrafish phenotype, due to the observed dramatic and irreversible impairments in tissues with cholinergic inputs. Further investigation revealed mechanistic similarities in the pathophysiological processes behind severe OPP between human and zebrafish (activation of the NMDA-receptor, inflammatory pathways and calcium dysregulation). Taking these findings into consideration, our goal in this work was to conduct a screening of potential molecules to be used in the prophylaxis and/or in the multifunctional treatment of the severe case of OPP. With this aim, we have combined standard treatment (atropine and pralidoxime) with molecules modulating pathways involved in OPP, such as NMDA-receptor antagonists (MK-801, memantine, caramiphen, benactyzine), anti-inflammatory drugs (dexamethasone and ibuprofen), calcium channel blockers (nifedipine and dantrolene), glutathione reserves replenisher (N-acetilycysteine) and nitric oxide synthase inhibitor (L-NAME).