Sarin attacks occurred both in Matsumoto and in Tokyo in 1994–1995; more than 15 people died because of such attacks. The acute toxic effect of Sarin nerve gas (organophosphorus: OP) produces miotic pupils as well as reduced cholinesterase (ChE) activities, which are nicotinic and muscarinic signs. A cholinergic sign may not be the sole mechanism of OP toxicity. Suzuki et al (1) described the following findings which are worthy of discussion: hypokalemia, depression of triglyceride, hypocapnea, change in electrolytes, etc.

Variance of clinical signs after the exposure is due to concentration, route of administration, age, sex, susceptibility and constitution of the enzymes to decompose Sarin. There were over 1,000 patients who had had contact with Sarin having severe sequlae. The delayed toxic effects of Sarin are, for example, depression, headache, fatigue and neuro-circulatory disturbances. The toxic effects such as 1) neurotoxicity 2) bronchial spasm and 3) cardiac toxicity are expected to last longer than other anticholinesterase compounds like DFP and phystostigmine (2).

OPs, including Sarin, act as secretagogues by inducing mast cell degranulation with associated autacoid release producing anaphylactoid reactions. Anaphylactoid shock can produce a lethal syndrome with symptoms of respiratory failure and circulatory collapse. Accumulated acetylcholine can act as an agonist of autacoid release, and autacoids such as histamine can augment anticholine esterase-induced bronchial spasm. In concert with dramatic cholinergic crisis in the acute OP toxicity, the precepts of neuroimmunology indicate that secondary adverse reactions encompassing anaphylactoid reactions may complicate OP toxicity (3).

Serum paraoxonase (PON) activity which resolves parathion into paraoxon has a biochemically unique characteristic. PON is closely relates to lipid metabolism. Reduced PON may produce arteriosclerosis (4). Thus, cardiac abnormality is frequently seen following acute OP intoxication. This may have a relationship to reduced PON by Sarin. Survivors after Sarin intoxication, still complain symptoms occurring in the central nervous system. In an experiment of neurotoxic study using animals, Sarin 5 μg/kg produced a moderate neurotoxic sign of the central nervous system with axonal degeneration of peripheral nerve followed by inhibition of neurotoxic esterase activity (5). OP has another important actions on the cell. The intracellular signal transduction process is the production of the intracellular messenger inositol triphosphate and the subsequent release of intracellular stores of calcium ion. After its production, inositol triphosphate is rapidly dephosphorylated and eventually the more stable product, inositol phosphate is formed. This rate of inositol phosphate formation, which can be measured in vitro, provides a general indication of the functional status of the intracellular second messenger system. In the animal study, the release of inositol phosphate was reduced by OP treatment (administration of fenthion), but unlike cholinesterase, it showed no substantial recovery over the 56th day test period even one administration of OP to the animals. This long-lasting change in the cholinergic signal transduction system in the nerve cell has several possible implications. Among the factors that could have produced this effect are a reduction in the number or function of muscarinic receptors, a reduction in the number of cells that contain muscarinic receptors or a change in the functional status of the intracellular second messenger system (6).

The after effect caused by Sarin intoxication is a significant matter in future study on non-cholinergic toxicity of nerve gas.

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References