EDITORIAL
DOI: 10.3904/kjim.2009.24.2.93

Clinical Outcome of Paraquat Poisoning

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The chemical composition of paraquat is $C_{12}H_{14}N_2$ and its molecular weight is 186.3. The lipid hydroperoxide induced by paraquat destroys cell membranes and kills the tissue of green plants via an oxidative process, which is initiated by the formation of superoxide as a result of the suppressed reduction of NADP in the course of photosynthesis when exposed to this herbicide. However, outside the living plant, this powerful superoxide is changed into a relatively inert chemical at high temperature or when exposed to soil mineral. Consequently, when paraquat is sprayed in the environment, it quickly loses its toxicity.

The first case of paraquat mortality was published in the British Medical Journal in 1966 [1]. In 1999, the Korean Agricultural Promotion Agency estimated that there were 800 deaths due to paraquat annually in Korea, while the Disease Control Center in Korea reported 256 cases in 2005 [2]. This implies that the mortality due to paraquat poisoning is decreasing, although the latest data were for a 9-month period and were collected from only 16 major domestic Emergency Centers.

Severely poisoned patients usually die of circulatory collapse quickly, although if the clinical course is prolonged, pulmonary fibrosis can develop. A paraquat dose of 30 mg/kg may be fatal. This is equivalent to 7-8 mL of the 24.6% solution sold commercially. With a dose of less than 7-8 mL, the survival rate is about 13% with no treatment, and increases to 73% with active treatment. Even with a dose exceeding 7-8 mL, the recent survival rate is as high as 50% with active treatment [3].

Most paraquat is absorbed in the jejunum; nevertheless, only 17.6% of it gets absorbed. This means that most resorption through the intestine is at a low rate. Despite this sluggish process, resorption through the small intestine may cause death. Therefore, urgent gentle gastric lavage is required to reduce the absorption and this should be followed by the administration of Fuller's earth and activated charcoal to inactivate the poison in the stomach. To expedite its excretion, laxatives, hydration, and diuretics should be started as soon as possible.

As the Proudfoot curve predicts, the plasma paraquat concentration is the factor with the greatest influence on the prognosis. The plasma paraquat concentration peaks within 2 hours and then decreases [4]. As the curve shows, the initial decrease is faster. This is called the distribution phase, and has a half life of about 5 hours and volume of distribution of 1.2-1.6 L/kg. The half life in the subsequent elimination phase is about 84 hours. A recent animal study reported that the paraquat concentration in severely poisoned pigs decreased with active excretion through the kidneys initially, but the plasma concentration increased progressively 2 hours later (the rebound phenomena) [5]. A persistent significant decrease in the concentration was observed with extracorporeal treatment, as compared to controls with no direct removal therapy. Therefore, extracorporeal treatment for Several days is highly recommended to reduce the paraquat level, and this would also prevent the rebound phenomena. In a severely poisoned individual with a high paraquat blood level, it takes at least 15 hours to reach the maximum level of paraquat in the lungs. The pulmonary concentrations can be 6 to 10 times higher than the plasma concentration. This means that the sooner extracorporeal treatment is initiated, the less paraquat reaches the lungs, and the procedure must be started within 15 hours. Some clinicians suspect the effectiveness of extracorporeal therapy and insist that maintaining renal function is the best policy, as the clearance rate of paraquat through the kidneys is high.

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However, nobody can guarantee that acute renal failure will not develop.

The best treatment is to initiate the most effective modality for removing paraquat from poisoned patients. Hemoperfusion is reported to be the most effective modality for clearing paraquat (116±32 mL/min) and detoxifying the poison. However, hemoperfusion is expensive and it is unlikely to remain effective for more than 6 hours for various reasons, such as thrombocytopenia. Hemodialysis (clearance 90±54 mL/min) and hemodiafiltration are less efficient, but allow a longer duration of continuous removal, for 2-5 days. Therefore, initial extracorporeal therapy with either hemodialysis or hemodiafiltration should be started as soon as possible and maintained for 2-5 days. The treatment is more effective when combined with hemoperfusion if possible. Hemofiltration is regarded as the least efficient treatment.

Lee *et al*. reported that patients surviving paraquat poisoning, who were discharged after finishing the initial rescue management, maintained good lung function without progressive deterioration for a long time, although the reason for this is not clear. In 2008, Yang examined the relationship between the serum total antioxidant status (TAS) levels measured in the emergency department and survival and concluded that the serum TAS on admission did not influence the clinical outcome significantly [6]. Yang suggested that the real defense comes from intracellular TAS. Very high doses of vitamins C and E on admission might increase the intracellular TAS, which might inhibit redox cycling and intracellular oxidation generation in the lungs. Kwon reported that antioxidant treatment improved the survival rate [7].

The activation of mononuclear macrophages by cell wall injury causes pulmonary fibrosis. Consequently, pulse therapy with methylprednisolone and cyclophosphamide is recommended to reduce the severity of inflammation and induce leukopenia to slow the process of pulmonary fibrosis. Noh reported the successful treatment of poisoned patients with therapy combining high-dose cyclophosphamide and steroid [8]. Eddlestone reported that anti-neutrophil therapy to prevent lung fibrosis did not necessarily give a better outcome [9].

In conclusion, the cases studied by Lee *et al*. showed that the late fibrotic process in the poisoned lungs may not be irreversible and progressive. A successful outcome requires initial aggressive treatment to control the serum paraquat concentration strictly. Active therapy with high-dose antioxidants and immunosuppressants might be very important for preventing the late progression. A large-scale randomized controlled trial is needed to examine this. **(Korean J Intern Med 2009;24:93-94)**

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