Whole lung lavage therapy: Treatment for lung injury caused by paraquat poisoning

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Paraquat poisoning is characterized by multi-organ failure and pulmonary fibrosis with respiratory failure, resulting in high mortality and morbidity. To serious paraquat patients, the effectiveness of conventional treatments is unsuccessful. Whole lung lavage is a technique that was developed in the 1960s with the purpose of removing lipoproteinaceous material that accumulates in the bronchi of patients with alveolar proteinosis, leading to clinical and functional improvement. Pneumoconioses are characterized as irreversible, progressive respiratory diseases. No effective therapy exists to prevent progression of these diseases. Whole lung lavage might limit the rate of disease progression through the removal of dust, inflammatory cells, and cytokines. Whole lung lavage is also used successfully to treat other lung diseases such as endogenous lipoid pneumonia and mineral oil lipid pneumonia. Paraquat poisoning could not be controlled by only one method and combined therapies are needed. So, we hypothesized that whole lung lavage will provide a new therapy of acute lung injury caused by paraquat. On the base of conventional therapy for paraquat poisoning, whole lung lavage could be considered in the early time of poisoning and then followed by glucocorticoid for patients with moderate to severe paraquat poisoning.

Key words: Paraquat, poisoning, acute lung injury, whole lung lavage.

INTRODUCTION

Paraquat is one of the most widely used herbicides in the world, and has been approved for use by authorities in more than 120 countries, and plays an important role in controlling weed in plantation estates. It is very popular in China countryside and widely used by Chinese farmers (Jian et al., 2008). On the other hand, paraquat is also a lethal poison. In China, paraquat is available and inexpensive, making poisoning prevention difficult. However, most of the people who become poisoned from paraquat have taken it as a means of suicide. So, paraquat is also a controversial herbicide, for it is highly toxic for humans (Kan et al., 2012). Intentional self-poisoning is the major reason for paraquat exposure and usually causes serious consequences in China (Shi et al., 2012). Paraquat poisoning is characterized by multi-organ failure and pulmonary fibrosis with respiratory failure,
resulting in high mortality and morbidity (Weng et al., 2012). Conventional therapy for paraquat poisoning both prevents further absorption and reduces the load of paraquat in the blood through haemoperfusion or haemodialysis. To serious paraquat patients, the effectiveness of standard treatments is unsuccessful (Liu et al., 2011). Paraquat mainly accumulates in the lung, and the main molecular mechanism of paraquat toxicity is based on redox cycling and intracellular oxidative stress generation (Huang et al., 2011). Immunosuppressive treatment using glucocorticoid and cyclophosphamide in combination is being developed and studied. But the effects of glucocorticoid with cyclophosphamide for patients with moderate to severe paraquat poisoning is limited (Li et al., 2010). Paraquat is actively taken up against a concentration gradient into lung tissue leading to pneumonitis and lung fibrosis. Paraquat also causes renal and liver injury. Activated charcoal and Fuller's earth are routinely given to minimize further absorption. Antioxidants such as acetylcysteine and salicylate might be beneficial through free radical scavenging, anti-inflammatory and NF-kB inhibitory actions. However, there are no published human trials. The case fatality is still very high in all centres despite large variations in treatment (Gawarammana et al., 2011).

**WHOLE LUNG LAVAGE**

Whole lung lavage is a technique that was developed in the 1960s with the purpose of removing lipoproteaceous material that accumulates in the bronchi of patients with alveolar proteinosis, leading to clinical and functional improvement. There has been an evolution in the technique; initially, it was performed under local anesthesia to each segment of the lung and currently it is performed under general anesthesia sequentially to both lungs (Aguiar et al., 2009). In brief, it involves the induction of general anesthesia followed by isolation of the two lungs with a double-lumen endotracheal tube and performance of single-lung ventilation, while large-volume lavages are performed on the non ventilated lung. Warmed normal saline solution in 1-L aliquots (total volumes up to 20 L) was instilled into the lung, and chest physiotherapy was performed. The proteinaceous effluent is drained with the aid of postural positioning. The sequence of events was repeated until such time as the effluent becomes clear. This procedure results in significant clinical and radiographic improvement secondary to the washing out of the proteinaceous material from the alveoli (Michaud et al., 2009). Whole lung lavage is considered the golden standard of pulmonary alveolar proteinosis treatment (Stoica et al., 2012; Rebelo et al., 2012). However, not all patients respond to this treatment. Based on the current literature, a stepwise treatment plan is suggested starting with WLL, continuing to inhaled GM-CSF, and then to rituximab if the former treatment regimes are unsuccessful (Leth et al., 2013; Yamamoto et al., 2008). Some authors think that the whole-lung lavage is a safe and effective palliative procedure in pulmonary alveolar proteinosis and in the treatment of patients with pulmonary disease, such as cystic fibrosis or asthma, in which filling of the lung acini by liquid or solid material impairs oxygenation of the pulmonary capillary blood (Lippmann et al., 1977). Pneumonitis is another lung disease that used whole-lung lavage as one of the major therapy in China (Zhang et al., 2012). Pneumoconioses are characterized as irreversible, progressive respiratory diseases. No effective therapy exists to prevent progression of these diseases. Whole lung lavage might limit the rate of disease progression through the removal of dust, inflammatory cells, and cytokines. Whole lung lavage is also used successfully to treat other lung diseases such as endogenous lipid pneumonia and mineral oil lipid pneumonia (Nicholson et al., 2002; Ceruti et al., 2007; Chang et al., 1993; Ciravegna et al., 1997).

**HYPOTHESIS**

Paraquat poisoning is an extremely frustrating clinical condition with a high mortality and with a lack of effective treatments in humans up to now. It is impossible for us stop person making use of paraquat, but some new therapy must be considered to control paraquat poisoning. Paraquat poisoning could not be controlled by only one method and combined therapies are needed (Lin et al., 2011). So, it was hypothesized in this study that whole lung lavage will provide a new therapy of acute lung injury caused by paraquat. Conventional therapy for paraquat poisoning both prevents further absorption and reduces the load of paraquat in the blood by using gastric lavage, catharsis, activated carbon adsorption, Fuller's earth inactivation, transfusion, dieresis, antioxidant, haemoperfusion or haemodialysis, etc. On the base of the earlier mentioned methods, whole lung lavage could be considered in the early time of poisoning and then followed by glucocorticoid for patients with moderate to severe paraquat poisoning.

**DISCUSSION**

Deliberate self-harm with pesticides is a significant public health problem in rural China. Even though many paraquat poisoning cases died in the past ten years in China, the pathological mechanisms of paraquat poisoning-induced acute lung injury were not well understood. A lot of clinical and basic research work has been done on paraquat poisoning in the past decade in our department (Zhao et al., 2010; Ning et al., 2010). This study developed and characterized a mouse model of paraquat-induced acute lung injury and studied the role of...
cytokines in the pathogenesis of paraquat poisoning (Xiangdong et al., 2011). Acute lung injury is characterized by three consecutive phases: exudative, proliferative, and fibrotic. In the exudative phase alveoli contain proteinaceous fluid, red blood cells, neutrophils, and macrophages. Edema and neutrophils accumulate in the interstitium, and alveolar ducts contain hyaline membranes. Microatelectasis is present, endothelial cells are swollen, and focal destruction of endothelial cells occurs (Meduri et al., 1996). The pathogenesis of acute lung injury involves various cytokines and growth factors (Gauldie et al., 1993). In the exudative phase, a number of presentations addressed the importance of the early response of proinflammatory cytokines, such as tumor necrosis factor (TNF)-α, interleukin (IL)-1, and interleukin (IL)-6 for their role in initiation of inflammation. The release of these cytokines into the alveolar space with diffusion to the vascular space in turn triggers diverse effects, including activation of the endothelium and circulating and resident leukocytes (Baughman et al., 1996; Metz et al., 1991). Studies have provided evidence for the importance of these cytokines in the pathogenesis of acute lung injury induced with paraquat (Ishida et al., 2006; Satomi et al., 2004). Abnormal expression of inflammatory cytokines is believed to play an important role in the pathogenesis of pulmonary fibrosis. So, thorough removal of inflammatory cytokines maybe a useful strategy to prevent further injury to the lungs. Whole lung lavage can remove the inflammatory seepage content from the lung tissue of paraquat poisoning at early stage, especially inflammatory factors. Therefore, it is recommend along with conventional therapies in the treatment of acute paraquat poisoning.

Conflict of Interests

The author(s) have not declared any conflict of interests.

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