Tropical Journal of Pharmaceutical Research August 2023; 22 (8): 1725-1731
ISSN: 1596-5996 (print); 1596-9827 (electronic)

Available online at http://www.tjpr.org
http://dx.doi.org/10.4314/tjpr.v22i8.26

Original Research Article

Efficacy of combined use of acetylcysteine and methylprednisolone in the treatment of paraquat poisoning

Yudan Yang, Pingping Zhou, Qingmian Xiao, Yongyan Han, Weizhan Wang, Yulan Yu*
Department of Emergency, Hengshui People's Hospital, Hengshui 053000, Hebei, China

For correspondence:* ***Email:* *yuyulan@halixun.com.cn*

Sent for review: 25 November 2022 *Revised accepted: 31 July 2023*

Abstract

Purpose: *To investigate the clinical impact of combined application of acetylcysteine and methylprednisolone in treating paraquat poisoning (PQP).*
Methods: *The clinical data of 92 PQP patients who received treatment in our hospital for 1 year were analyzed. The patients were equally divided into control group (CG) and study group (SG), based on treatment plans. All patients underwent routine acute-phase treatment, while SG was additionally treated with acetylcysteine in combination with methylprednisolone. After treatment, the renal function, pulmonary fibrosis indices and inflammatory factor levels of both groups were determined.*
Results: *During the 1 - 4 weeks of treatment, there was no statistical difference in the survival rates of patients at various time periods ($p > 0.05$). After treatment, there were markedly lower levels of blood urea nitrogen (BUN) and serum creatinine (SCr) in SG than in CG. There was lower incidence of pulmonary fibrosis in SG than in CG, although the difference was not significant. Patients in SG had lower HRCT scores and levels of C-reactive protein (CRP), interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) than those in CG ($p < 0.05$).*
Conclusion: *Acetylcysteine in combination with methylprednisolone significantly reduces the degree of pulmonary fibrosis and improves renal function and inflammatory levels. It has a positive implication for early treatment of patients, especially for the prognosis of patients with mild-to-moderate poisoning. Therefore, the combined therapy has potential for clinical application.*

Keywords: *Acetylcysteine, Methylprednisolone, Paraquat, Poison*

Tropical Journal of Pharmaceutical Research is indexed by Science Citation Index (SciSearch), Scopus, Web of Science, Chemical Abstracts, Embase, Index Copernicus, EBSCO, African Index Medicus, JournalSeek, Journal Citation Reports/Science Edition, Directory of Open Access Journals (DOAJ), African Journal Online, Bioline International, Open-J-Gate and Pharmacy Abstracts

INTRODUCTION

Paraquat is a non-selective contact herbicide that accumulates as toxin in multiple organs of the human body after inhalation via the alimentary tract, skin or respiratory tract. The highest amount of toxin is accumulated in the lungs, resulting in acute lung injury, acute respiratory distress syndrome and multiple organ dysfunction. At present, no good antidote has been found. Thus, paraquat exposure results in high clinical mortality. At present, a clinical study has shown that paraquat not only causes physical damage under physicochemical effect but also causes multiple organ dysfunction in combination with cytokines and inflammatory

factors, thereby accelerating disease progression [1]. Therefore, clinical treatment for PQP involves mainly toxin clearance, antioxidant treatment, protection of important organs, prevention or reduction of pulmonary fibrosis, and other comprehensive treatment measures [2].

Methylprednisolone, a steroid hormone with strong anti-allergic, anti-inflammatory and immunosuppressive effects, inhibits, to some degree, allergy to autoimmune system caused by viruses, but it also reduces the defense function of the human immune system, indicating certain limitations during individual use [3]. Acetylcysteine is characterized by free radical scavenging. It is frequently used as an antioxidant in clinics and as a precursor of reduced glutathione *in vivo.*

Acetylcysteine has antioxidative and strong anti-inflammatory effects; it protects the pulmonary epithelial cells from injury while reducing the levels of inflammatory factors. Some studies have shown that acetylcysteine, in combination with methylprednisolone, may be used for the treatment of radiation-induced lung injury, but its efficacy in treating pulmonary fibrosis caused by paraquat poisoning (PQP) has not yet been reported [4,5]. Therefore, in this study, the clinical effects of acetylcysteine in combination with methylprednisolone in the treatment of PQP were retrospectively analyzed. The PQP subjects were PQP patients in *Hengshui People's Hospital* who were treated with a combination of acetylcysteine and methylprednisolone.

METHODS

Inclusion criteria

Patients with paraquat poisoning consistent with the diagnostic criteria of PQP [6]; patients who received medical treatment in *Hengshui People's Hospital* for the first time, and patients with complete clinical data, were included in this study. The study was approved by the Ethics Committee of Hengshui People's Hospital (approval no. 20210133). Signed written informed consent was obtained from the patients and/or guardians. This study was conducted in line with the Declaration of Helsinki [7].

Exclusion criteria

The excluded patients were those who took paraquat in excess of 50 mL; patients with the poisoning of the skin or respiratory tract, patients who did not receive treatment more than 16 h after poisoning, those with a history of pulmonary inflammatory diseases, patients who died or gave up treatment in the short term, those with dysfunctions in liver, kidney and heart, patients who had contraindications to drugs used in this research, and those who were poisoned with other drugs.

Sample size and grouping

The PQP patients were retrospectively and equally assigned to 2 groups: control group (CG) and study group (SG), on the basis of treatment. All subjects underwent routine acute-phase treatment, while SG was additionally treated with acetylcysteine in combination with methylprednisolone.

Treatments

The treatment methods in CG were as follows: firstly, gastric lavage and whole gastric and bowel irrigation were performed. On the basis of doctor's advice, 60 g of montmorillonite powder was added to 15000 - 30000 mL of gastric lavage fluid. One-time gastric lavage was done using an electric gastric lavage machine, and then whole gastric and bowel irrigation was repeatedly performed through an indwelling nasal-stomach tube. A total of 30 g of activated carbon was fully dissolved in 200 mL of warm water and then injected into the stomach from the gastric tube. Two boxes of polyethylene glycol electrolytes powder were dissolved in 2000 mL of warm boiled water (at a temperature not exceeding 30 °C), and then injected into the gastric tube for whole bowel irrigation, twice a day for three days [8]. Regarding blood purification, the hybrid model of hemoperfusion and continuous venovenous hemofiltration (CVVH) was carried out, and CVVH was continued for patients with renal insufficiency until their urine volume and renal function returned to normal. Finally, patients received intravenous infusion and symptomatic and supportive treatment, including intravenous infusion of cyclophosphamide, high-dose vitamin C and ulinastatin, and orally administered propranolol for symptomatic and supportive treatment. Besides, patients who had respiratory and circulatory failure were given necessary circulatory support and respiratory ventilation [9].

Patients in SG were additionally treated with acetylcysteine in combination with methylprednisolone. In the first two weeks, 8 g of acetylcysteine (manufacturer: Zambon Italia S.R.L.; specification: 8 g; approval No. H20070264) was injected through intravenous drip twice a day. After two weeks, the patients were given acetylcysteine tablets (manufacturer: Hainan Zambon Pharm. Co. Ltd.; specification:

0.2 g; approval No. H20080326) at an oral dose of 0.2 g three times daily, for two months. Methylprednisolone (500-1000 mg) was intravenously given daily in the first five days. Then, the medication dose was adjusted according to the actual situation of the patients.

Evaluation of parameters/indices

General information such as age, BMI, treatment time, APACH II scores, plasma concentration, gender and organ injury were retrieved from medical records for comparison and analysis. The survivors in the first, second, third and fourth weeks of treatment were counted so as to calculate the survival rate in each period.

Renal function indices such as levels of blood urea nitrogen (BUN) and serum creatinine (SCr) were measured before and after treatment. Moreover, CT scanning was performed on the patients during the first, second, third, and fourth weeks of treatment. The HRCT score was used to evaluate pulmonary CT images, and the semi-quantitative score was obtained according to the percentage of the cumulative shadow area of the signs in the lung lobe at the same layer. The severity of pulmonary fibrosis was classified into 4 grades based on the scores: normal lungs (0 points), mild fibrosis (1 - 5 points), moderate fibrosis (6 - 10 points) and severe fibrosis (> 10 points).

In the fasted state, early morning venous blood (3 mL) was taken from each patient and centrifuged at 3000 rpm for 15 min, to obtain serum. Before and after treatment, the serum levels of inflammatory factors i.e., C-reactive protein (CRP), interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) in patients were assayed using ELISA.

Statistical analysis

The differences between the two groups were calculated with SPSS 22.0, and GraphPad Prism 7 was employed for drawing graphs. Enumeration and measurement data obtained are presented as n (%) and mean ± standard deviation (SD), respectively, and were statistically analyzed with χ^2 test and *t*-test, respectively. Values of $p < 0.05$ indicated statistically significant differences.

RESULTS

Basic clinical data

There were no significant differences in the basic data such as age, BMI, treatment time, APACH II scores, plasma concentration, gender and organ injury between the two groups ($p > 0.05$; Table 1).

Survival rates

Figure 1 shows that at weeks 1, 2, 3 to week 4, there were 38, 31, 29, and 28 survivors in CG, and 39, 34, 32, and 30 survivors in the SG, respectively, demonstrating no marked differences in the survival rates of patients at the different time periods ($p > 0.05$).

Kidney function

After treatment, the SG had significantly lower serum levels of BUN and SCr than CG ($p < 0.05$). However, prior to treatment, BUN and SCr levels were comparable in the 2 groups ($p > 0.05$; Table 2).

Table 1: Comparison of general information (n = 46)

Indices	CG	SG	χ^2/t	*P*-value
Age (years)	32.76±5.17	34.55±6.20	1.504	0.136
BMI (kg/m^2)	24.11±3.05	24.08±3.01	0.047	0.962
Treatment time (h)	1.92±0.11	1.96±0.10	1.825	0.071
APACH II scores	8.56±4.12	9.24±4.37	0.768	0.445
Plasma concentration (mg/L)	5.60±2.05	5.41±1.97	0.453	0.652
Gender			0.044	0.834
Male	25(54.35)	26(56.52)		
Female	21(45.65)	20(43.48)		
Organ injury				
Respiratory failure	4(8.70)	5(10.87)	0.123	0.726
Liver injury	2(4.35)	1(2.17)	0.345	0.557
Kidney injury	1(2.17)	1(2.17)	0.000	1.000
Myocardial injury	2(4.35)	3(6.52)	0.212	0.646
Educational status			0.058	0.810
Below high school	11(23.91)	12(26.09)		
High school and above	35(76.09)	34(73.91)		

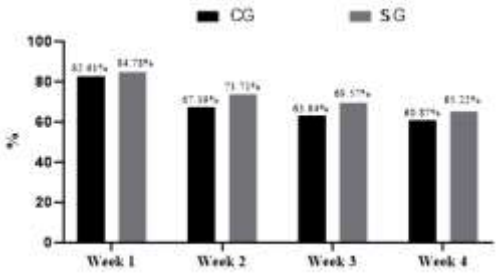

Figure 1: Statistics of survival rates at different time periods

Pulmonary fibrosis indices

During the 4 weeks of treatment, the incidence of pulmonary fibrosis was lower in the SG than in CG, although the incidence was comparable in both groups. Patients in SG had significantly lower HRCT scores than those in CG ($P < 0.05$). These results are shown in Tables 3 and Table 4.

Levels of inflammatory factors

Before treatment, there were no significant differences in levels of CRP, IL-6 and TNF-α between the two groups. However, after treatment, the levels of CRP, IL-6 and TNF-α were lower in SG than in CG ($p < 0.05$). These data are presented in Table 5.

DISCUSSION

Paraquat, an efficient contact herbicide, accumulates mainly in the lungs after entering the blood through absorption, thereby causing lung injury. In particular, irreversible pulmonary fibrosis is easily formed in the late stage of PQP, which in turn leads to respiratory failure, an important cause of death in PQP patients [11,12].

Table 2: Levels of renal function indices

Group	BUN (mmol/L)		SCr (μmol/L)	
	Before treatment	After treatment	Before treatment	After treatment
CG	9.51±1.07	7.12±1.23	212.86±16.20	150.91±10.22
SG	9.53±1.06	5.19±1.18	211.85±16.08	130.76±9.11
t	0.090	7.680	0.300	9.982
P-value	0.928	<0.001	0.765	<0.001

The normal range of BUN is 3.2 - 7.1 mmol/L, while the normal range of SCr is 44 - 133 μmol/L [10]

Table 3: Statistics of pulmonary fibrosis

Period		CG	SG	χ^2	*P*-value
Week 1	Survivors (n)	38	39		
	Lung fibrosis cases (n (%)	35 (92.11)	35 (89.74)	0.130	0.719
Week 2	Survivors (n)	31	34		
	Lung fibrosis cases (n (%))	28 (90.32)	30 (88.24)	0.074	0.786
Week 3	Survivors (n)	29	32		
	Lung fibrosis cases (n (%))	26 (89.66)	28 (87.5)	0.070	0.792
Week 4	Survivors (n)	28	30		
	Lung fibrosis cases (n (%))	25 (89.29)	26 (86.67)	0.094	0.760

Table 4: Statistics of HRCT scores

Period	CG	SG	χ^2	*P*-value
Week 1	4.01±0.29	3.15±0.36	12.618	<0.001
Week 2	9.74±0.57	8.59±0.80	7.940	<0.001
Week 3	11.37±0.57	9.10±0.94	14.005	<0.001
Week 4	10.41±0.61	9.50±0.85	5.899	<0.001

Table 5: Statistics of inflammatory factor levels

Group	CRP (mg/L)		IL-6 (pg/mL)		TNF-α (pg/mL)	
	Pre treatment	Post treatment	Pre treatment	Post treatment	Pre treatment	Post treatment
CG	43.87±4.52	36.55±3.17	12.55±1.08	8.30±1.11	22.97±2.23	16.72±1.40
SG	44.10±4.73	20.81±3.03	12.58±1.05	5.04±1.02	22.84±2.25	11.58±1.10
t	0.238	24.344	0.135	14.667	0.278	19.580
P-value	0.812	<0.001	0.893	<0.001	0.781	<0.001

The mechanism of paraquat poisoning is still unknown, but based on previous studies, oxidative stress, inflammatory injury and calcium dyshomeostasis may be the main pathogenic mechanisms. However, abnormal gene expression, mitochondrial damage, loss of alveolar surfactant, and the imbalance in cytokine network and enzymes, also play important roles [13]. Typically, PQP presents acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) in the early stage, and then gradually causes fibrosis in the alveoli and lung interstitium, which in turn may lead to death of the patient.

Acetylcysteine is deacetylated to glutathione, a precursor of reduced glutathione, thereby increasing the concentrations of GSH in patients and enhancing the antioxidant potential of cells *in vivo*. Previous studies have also suggested that acetylcysteine directly acts as an antioxidant in humans, protects pulmonary tissues from oxidative damage by oxygen free radicals, reduces the degree of pulmonary fibrosis, and inhibits inflammatory response [14]. Methylprednisolone is a steroid hormone which effectively inhibits a variety of cytokines and inflammatory factors, enhances the anti-inflammatory and anti-immune ability of patients, reduces the activity of macrophages and collagen, exerts anti-inflammatory effects, maintains the stability of cytomembrane, and protects lung tissues [15].

In the present study, no significant differences were observed in the survival rates of patients at different time periods during the 4 weeks. In the 4 treatment weeks, the incidence of pulmonary fibrosis was lower in SG than in CG, with no significant difference between the two groups, while the HRCT scores were markedly lower in SG than in CG. Moreover, the results showed that acetylcysteine in combination with methylprednisolone did not markedly reduce the mortality rate of patients, and had no effect on the occurrence of pulmonary fibrosis, but it markedly decreased the degree of pulmonary fibrosis. This indicates that the combined therapy has promising potential for clinical treatment of PQP patients.

Paraquat is one of the most effective herbicides, and it has the highest toxicity among pesticides. Patients who are exposed to high doses of paraquat often die from multiple organ failure within a short time. Indeed, even if the dose taken is relatively small, there is still a certain degree of organ damage. Paraquat poisoning (PQP) rapidly triggers systemic inflammatory response, promotes the activation of coagulation factors, and inhibits anticoagulation and fibrinolysis, thereby resulting in the formation of microthrombus in organs, reduced renal blood flow, and renal impairment. In addition, lung injury causes renal and myocardial hypoxia, and weakens heart rate, leading to decreased renal blood perfusion, aggravated renal injury, and kidney failure. In the kidneys, paraquat directly acts on epithelial cells of kidney tubules and generates massive amounts of oxygen free radicals, resulting in cellular oxidative damage. Moreover, calcium ion overload triggers damage and apoptosis of epithelial cells of kidney tubules [16].

Therefore, free radical-induced damage is one of the important factors in the pathogenesis of renal injury in PQP. Impaired renal function is also crucial in prognosis of PQP patients. This study demonstrated that SG had lower levels of BUN and SCr after treatment than the CG. Thus, acetylcysteine in combination with methylprednisolone effectively improved the renal function indices of PQP patients and effectively enhanced the tolerance of patients to paraquat toxicity.

The antioxidant effect of acetylcysteine inhibits the production of oxidative free radicals in patients, antagonizes paraquat-induced renal injury, maintains homeostasis, and facilitates the recovery of renal function, in combination with anti-inflammatory effect of methylprednisolone. Clinical experiments have found that the renal injury induced by PQP is reversible. This provides a realistic basis for correcting renal pathological injury in clinics, and it facilitates complete clearance of paraquat. It can be seen that the combination of acetylcysteine and methylprednisolone produced a positive impact on the prognosis of PQP patients [17].

Inflammatory reaction plays an important role in the pathogenesis of PQP. At the early stage of poisoning, the effector cells of paraquat release a large number of inflammatory factors such as CRP, IL-6 and TNF-α. These mediators enhance the infiltration, differentiation and maturation of inflammatory cells to form a huge cytokine network which impairs immune function, ultimately leading to systemic inflammatory response syndrome and multiple organ failure. When PQP occurs in patients, the accumulation of a large number of toxins in organs such as lung and kidneys produce inflammatory mediators which trigger a series of oxidative stress reactions, with the aggravation of inflammatory reactions. The accumulation, activation and infiltration of inflammatory cells further aggravate organ damage and lead to

death in severe cases. Therefore, inflammation is one of the main mechanisms involved in PQP-induced organ damage.

This study showed that SG had lower levels of CRP, IL-6 and TNF-α than CG, which is consistent with the findings of Firouzian [18]. This confirms that PQP led to infiltration of a large number of inflammatory factors in the patients, while acetylcysteine in combination with methylprednisolone effectively reduced the inflammatory response. Acetylcysteine is metabolized to reduced glutathione which participates in the redox process *in vivo* and neutralizes superoxide anion *in vivo* through oxidative decomposition, thereby reducing oxygen free radical-induced injury to body tissues. In addition, after combination with other free radicals *in vivo*, inactivated thiols are converted to easily metabolizable acidic materials and excreted from the body.

Thiols also effectively improve tissue antioxidant capacity and reducing power, and inhibit the activation and production of a variety of inflammatory factors, thereby exerting anti-inflammatory effects. Methylprednisolone has strong anti-inflammatory and anti-allergic properties, and it inhibits virus-induced allergic reactions in the autoimmune system, thereby reducing pulmonary cell injury caused by an inflammatory response. In this study, acetylcysteine in combination with methylprednisolone inhibited inflammation, and reduced the production of lipid peroxides, thereby exerting a synergistic effect.

Limitations of the study

The limitations of this study are as follows: firstly, for a retrospective study, the sample size was small. In addition, the physical and mental states of patients during this study might have influenced the data reported. Therefore, follow-up studies are necessary to actively carry out prospective studies for deep analysis using an expanded sample size. Moreover, this study focused on the analysis of short-term efficacy.

CONCLUSION

Acetylcysteine in combination with methylprednisolone did not significantly improve the survival rate of PQP patients, nor did it significantly reduce the incidence of pulmonary fibrosis. However, this combined therapy significantly decreases the degree of pulmonary fibrosis, improves renal function, reduces inflammatory factor levels, and had a positively significant effect on early treatment of patients, especially for the prognosis of patients with mild-to-moderate poisoning. Therefore, follow-up studies should focus on the long-term efficacy and impact on patients, for clinical reference.

DECLARATIONS

Acknowledgements

None provided.

Funding

None provided.

Ethical approval

None provided.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

We declare that this work was done by the authors named in this article, and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Yudan Yang and Yulan Yu conceived and designed the study, and drafted the manuscript. Yudan Yang, Pingping Zhou, Qingmian Xiao, Yongyan Han and Weizhan Wang collected, analyzed and interpreted the experimental data. Yudan Yang and Pingping Zhou revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

REFERENCES

1. Yin Y, Shen H. Melatonin ameliorates acute lung injury caused by paraquat poisoning by promoting PINK1 and BNIP3 expression. Toxicol 2023; 490: 153506.
2. Xiong G, Zhao L, Yan M, Wang X, Zhou Z, Chang X. N-acetylcysteine alleviated paraquat-induced mitochondrial fragmentation and autophagy in primary murine neural progenitor cells. J Appl Toxicol 2019; 39: 1557-1567.
3. Liang B, Feng X, Deng R, Liu Y, He Y, Zhang X. Efficacy and safety of post-auricular injection of methylprednisolone sodium succinate and lidocaine in the treatment of acute tinnitus, and its effect on sleep quality. Trop J Pharm Res 2022; 21: 1079-1085.
4. Guo J, Wang P, Ma X. Effect of acetylcysteine solution combined with fiberoptic bronchoscopy alveolar lavage in elderly patients with severe ventilator-associated pneumonia. Trop J Pharm Res 2021; 20: 1061-1066.
5. Hisamura M, Ogura T, Tokuda M, Nakamura M, Kenichiro S, Ando Y, Nakata K, Taguchi H. A case of severe paraquat poisoning treated by continuous hemodiafiltration without sequelae. Acute Med Surg 2023; 10: e833.
6. Zhang Z, Nian Q, Chen G, Cui S, Han Y, Zhang J. Klotho alleviates lung injury caused by paraquat via suppressing ROS/P38 MAPK-regulated inflammatory responses and apoptosis. Oxid Med Cell Longev 2020; 2020: 1854206.
7. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA 2013; 310: 2191-2194.
8. Gao YX, Wang YB, Wan YD, Sun TW, Li Y, Hou LL, Sun P, Yuan D, Duan GY, Sun CH, Che L, Zhang Y. Immunosuppressive drugs to reduce the mortality rate in patients with moderate to severe paraquat poisoning: A Meta-analysis. J Toxicol Sci 2020; 45: 163-175.
9. Gawarammana I, Buckley NA, Mohamed F, Naser K, Jeganathan K, Ariyananada PL, Wunnapuk K, Dobbins TA, Tomenson JA, Wilks MF, et al. High-dose immunosuppression to prevent death after paraquat self-poisoning - a randomized controlled trial. Clin Toxicol (Phila) 2018; 56: 633-639.
10. Vinod SS, Reed AB, Maxwell J, Cron RQ, Stoll ML. Pediatric rheumatology infusion center: report on therapeutic protocols and infusions given over 4 Years with focus on adverse events over 1 Year. Pediatr Rheumatol Online J 2018; 16: 16.
11. Su YW, Liu YM, Zhang JW, Zhou LL, Du WJ, Wang Z. The risk prediction value of paraquat poisoning dose, urine protein and myocardial enzymes. Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za Zhi 2023; 41: 8-13.
12. Su W, Dong Q, Jiao F. Study on the efficacy and safety of ambroxol combined with methylprednisolone in patients with acute lung injury. Biomed Res Int 2021; 2021: 5771101.
13. Gao Y, Guo S, Wang Y, Yu S, Wang M, Lu X, Li Y. Lymphocyte and its CD4+ and CD8+ subgroup changes after paraquat poisoning. Hum Exp Toxicol 2019; 38: 1024-1030.
14. Gao YX, Wang YB, Wan YD, Sun TW, Li Y, Hou LL, Sun P, Yuan D, Duan GY, Sun CH, et al. Immunosuppressive drugs to reduce the mortality rate in patients with moderate to severe paraquat poisoning: A Meta-analysis. J Toxicol Sci 2020; 45: 163-175.
15. Montoya-Giraldo MA, Díaz LF, Gómez UE, Quintero J, Zuluaga AF. Use of low-molecular-weight heparin in severe paraquat poisoning: a case report. J Med Case Rep 2020; 14: 240.
16. Zhao X, Xiao Y, Zhu J, Xu Z, Liu L, Zhang J. Prognostic comparison of goal-oriented hemoperfusion and routine hemoperfusion combined with continuous venovenous hemofiltration for paraquat poisoning. J Int Med Res 2018; 46: 1091-1102.
17. Wu Q, Xu Q, Jian X, Wang H, He X, Gao B, Wang K, Kan B. A new sight for paraquat poisoning from immunology. Immunopharmacol Immunotoxicol 2018; 40: 269-272.
18. Firouzian F, Pourshoja P, Nili-Ahmadabadi A, Ranjbar A. Hepatoprotective effect of N-acetylcysteine loaded niosomes on liver function in paraquat-induced acute poisoning. Pestic Biochem Physiol 2019; 160: 146-153.