# Paraquat intoxication: a review

Rita Monteiro, Lurdes Correia, Adélia Simão, Armando Carvalho, Nascimento Costa

**Abstract**

Paraquat is a very toxic herbicide still available in Portugal and a cause of many deadly cases. The diagnosis is emergent and sometimes complex. The prognosis is poor, mainly in cases of high doses intoxication as there is no proven effective therapy. The authors review the pharmacokinetics, mechanism of action, clinical manifestations, available therapies and prognostic factors. They highlight the low sensitivity of urine Paraquat test in diagnosis and the importance of blood Paraquat test in the prognosis. Finally, a call for the development of research leading to new therapies is made.

Key words: Paraquat, poisoning, review, urine Paraquat test..

## INTRODUCTION

Paraquat (1,1 dimethyl – 4, 4 – bipyridinium dichloride) is a contact herbicide in the format of a water solution 20% (200 + 10 g/L). [1] It is commercially known as Gramaxone SYNGENTA®, Paraquato SAPEC® or Paraquato SELECTIS or Paraquato SELECTIS®, Gramocil®, Agroquat®, Gramuron® or Paraquol®.

In spite of being forbidden its marketing by the European Union in July 2007, [2] this herbicide is still available, mainly in the countryside where some farmers still have leftovers, acquired before being forbidden and still use it, due to its efficacy. A part of that, some traders have this product in stock, as they did not manage to sell it before being forbidden and eventually they can try to sell, under the counter.

It is not explosive or inflammable. It is corrosive for metals and decomposes itself when exposed to ultraviolet radiation. Its advantages are in the low-cost, high efficacy and absence of pollutant effect for the soil, and it does not accumulate in the food chain.[3,4] Unfortunately, the unduly use of such herbicide has led to a number of intoxication cases, most of them lethal, due to the absence of an actually effective treatment.

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## PHARMACOKINETICS AND ACTION MECHANISM

The mean lethal dosage is estimated in 10 – 20 mL of Paraquat solution at 20% (2 – 4 g),[3,4] but it can be lower or higher, depending on the individual previous health condition. Therefore higher the number of previous comorbidities, less is the capacity of the individual to respond to Paraquat aggressions in different organs and consequently, higher will be the probability of intoxication with a fatal outcome, which doses lower than then the lethal doses.[3,5] From the total amount of Paraquat ingested, only 5 -20% is absorbed. [1,6] It is not metabolized in the liver and id does not bind to serum proteins making its distribution volume very high. [3] The average serial peak occurs around two hours after being ingested, but it can vary between 30 minutes and four hours, depending on individual.[1,6] Its elimination is made through the digestive system, with the presence of 80% of herbicide unchanged in the stools and only 15% excreted in the urine, by glomerular filtration and active tubular secretion.[3] Paraquat is also is excreted in the bile.[2,5] The excretion through the biliary route seems to be due to the strong presence of the P-glycoprotein involved in carrying Paraquat.[2] Paraquat presence in biliary samples got post-mortem and the cholestatic lesions associated to the intoxication by Paraquat supports such statement. [2,5] In most cases the intoxication occurs by oral route but it can also occur by transdermal route when there is a loss on the skin integrity.[3,5] The intoxication by inhalation usually does not cause harmful effects.[3] Paraquat disappears on the plasma five – six hours after being ingested, binding to the tissues and it is excreted in the urine.[7]

Paraquat toxicity results of its enormous capacity to react with oxygen, leading to the formation of

free radicals highly harmful for the cells, namely the superoxide anion, through the multiple reactions of oxidation – reduction.[3,4]

Paraquat binds to the tissues, namely the most vascularised is quick and early.[6] The lung is one of the most affected organs in an early stage (+ 4 hours after ingestion)[1,4] and where the toxic effect is the highest, as it is the area with the highest oxygen concentration and subsequently, where there are the highest levels of Paraquat. After binding to the tissues there is a rebound effect, i.e., there is a slow diffusion of Paraquat in the tissue to the blood when it is serial levels decrease, leading to a new increase on Paraquat in blood values.[6,8]

Therefore there is a need of keeping the therapy, even when Paraquat in the blood is untraceable.

## CLINICAL MANIFESTATIONS

Paraquat affects all systems of the human organism.

In the oropharynx and esophagus it causes edema and pain, with mucosa peeling, exudation and ulceration and seldom esophagus perforation.[1] Nausea, vomiting (often induced by an emetic agent added to the Paraquat formulation),[4] abdominal pain (mainly epigastralgia) and diarrhoea occur.

The ingestion of high doses can lead to severe liver lesions, with fat degeneration of periportal hepatocytes, cholestasis, portal inflammation and central necrosis of hepatic lobes associated to edema, degenerescence and necrosis of biliary channels, both intra- and extrahepatic and of the gallbladder.[3] Some authors describe two phases in the hepatotoxicity by Paraquat: the first, related with the accumulation of such herbicide, conditioning hepatocellular lesions; the second one causes cholestatic lesions, due to the excretion of Paraquat through the bile or being absorbed through the entero-hepatic circulation, with a subsequent elimination in the bile. [2]

In the respiratory system there is a loss of alveoli epithelial cells and pneumocytes type I and two, fibroblast proliferation, absence of surfactants secretion, thickening of the alveoli walls due to interstitial fibrosis, increased capillary permeability, hypoxaemia and reduction of lung volumes, dyspnoea with progressive deterioration and subsequently, respiratory failure.[3,4]

At renal level, Paraquat accumulation occurs mainly in the proximal convoluted tubules, leading to acute tubular necrosis. [3,4,9] Pathophysiology of the renal lesion is not clear but lesions occur later than the pulmonary ones. Paraquat excretion has two stages: one, an early and quick one and a second one, later, slower, due to the tissular redistribution and affected by the eventual kidney dysfunction. [4]

When this happens, the prognosis is worst, [4] as renal insufficiency develops with a reduction of Paraquat excretion and a higher accumulation in the lung. Fanconi syndrome can also occur with aminoaciduria, glycosuria, increase on sodium, phosphorus and uric acid excretion.

Toxic myocarditis, followed by shock and dysrhythmias is another side effect.

Paraquat crosses the blood-brain barrier, destroying mainly the dopaminergic neurons of the corpus striatum, generating anxiety, seizures, ataxia, awareness reduction, hemorrhage and focal demyelinization.

Adrenal necrosis may exist.

The mortality rate of individuals intoxicated by Paraquat is usually from 63% 70% [4] and the survival period is low, both depending on the ingested and absorbed dose, the eventuality of emerging an acute renal insufficiency and the absence of an actually effective treatment. [2] A study points out for a mortality rate of almost 100% in the case of being ingested a dose higher then 40 – 45 mg/kg.[7] For a higher ingestion an early death (1 to 4 days), secondary to edema and pulmonary hemorrhage, hepatocellular and adrenal insufficiency. [3] With lower doses death occurs later, from 4 days to several weeks after ingestion, due to the progressive onset of multiple organic insufficiencies, mediastinitis, treatment complications and pulmonary fibrosis. [3]

## PROGNOSIS DETERMINANT FACTORS

The main factors determining prognosis are the concentrations involved (whether or not diluted), the dosage, the intoxication routes, starting an early treatment, the reduction of the intestinal absorption, the renal function, Paraquat values in the urine and in the blood.[3,5]

It is verified that the absorption decreases the presence of food in the stomach, vomits, undergoing stomach washing, administration of emetic and adsorption agents, or forced diarrhoea and increasing if there are esophagus-gastric ulcers.[3,5,7]

A delay starting the treatment above, higher than 2-5 hours and the existence of previous changes of the

renal function, or the early onset of acute renal insufficiency, reduce drastically the probability of survival.[3]

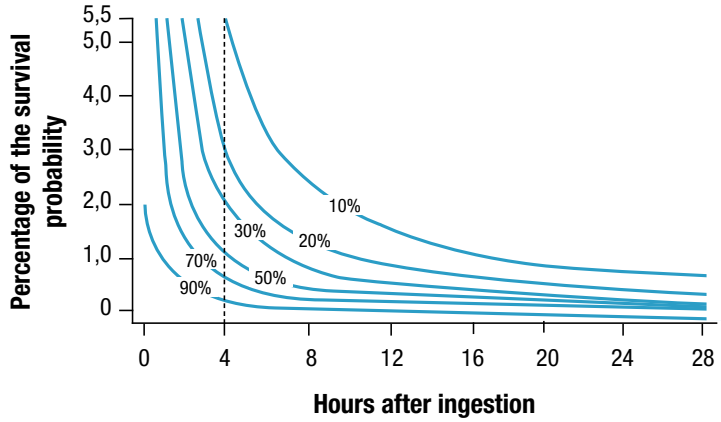
Paraquat can be dosed in the urine, serum, gastric and dialysis aspirate.The presence of Paraquat in the urine is detected through a semiquantitative test with sodium dithionite 1% in alkaline solution, changing the urine color to blue when the Paraquat concentration is higher than 0.5 µg/mL, with a darker tone as higher is the product concentration.[10] However in spite of being useful, it is not very sensitive and very limited because it does neither detect Paraquat levels below 0.5µg/mL, nor does it allow establishing the dosage.

Urine should be tested for 24 hours after ingestion,[3,5,7] but a negative result should be construed carefully, as this test performed in an early stage can underestimate the quantity of absorbed Paraquat. A part of that, in a case of acute renal insufficiency Paraquat excretion is reduced, and the results can be falsely untraceable. The ideal would be to quantify Paraquat in the urine, using spectrophotometry. In a study of Paraquat urinary excretion in 16 patients, the conclusion reached was that the intoxication was lethal when the excretion was higher than 1 mg/h for 8 hours or more after ingestion.[3]

If Paraquat is not detected in the urine, the approach is very controversial. Some authors argue that when there is a strong clinical suspicion, treatment should be early and appropriate even with untraceable Paraquat in the urine.[11] Others advocate to repeat the Paraquat urine test six hours afterwards, and if this second dosage is still untraceable, it should be excluded the hypothesis of intoxication by Paraquat.[5]

There are those who think that if Paraquat urine test is undetectable for 24-hours then it is unlikely to be a lethal intoxication.[5]

In a study carried out by Sae-Yong et al.,[12] where 147 patients were included, intoxicated by Paraquat, 54 had untraceable Paraquat in the urine test and from these five died. In another study carried out by Hiroshima Nagami et al,[11] with 79 patients intoxicated with Paraquat, two had untraceable Paraquat in the urine, but from these two, one ended up dying leading these authors to think about an early and appropriate treatment, even with untraceable Paraquat in the urine. In our experience, we also had a patient who died by Paraquat intoxication, showing untraceable values of Paraquat in the urine, 11 and 168 hours, but with traceable Paraquat in the blood.[13]




Percentage of an individual survival probability after taking Paraquat through the correlation of plasmatic concentration in mg/ml and the time in hours after ingestion, according to Hart et al.[5]

FIG. 1

Therefore it is advocated the use of the Paraquat blood test as the most sensitive exam. It should be determined before starting therapy and it is the most reliable prognosis factor. Serial Paraquat levels considerably lethal are those above 2 µg/mL at four hours, 1.6 µg/mL at 12 hours, 0.6µg/mL at 16 hours and 0.16 µg/mL at 24 hours.[1] An individual probability of survival after taking Paraquat can also be supplied through the correlation of plasmatic concentration (in µg/mL) overtime (in hours) after ingestion, according to the normogram of Hart et al (*Fig. 1*).[5]

Schermann et al,[14] widened this predictive curb of 28 hours for seven days after the ingestion demonstrating that patients with values of Paraquat in the blood of 10µmg/mL in the first eight hours would die early, usually within 24 hours, of cardiogenic shock and those with lower concentration but above the predicted line, would die later, after 24-hour, with pulmonary fibrosis and respiratory failure.[5]

Dosing Paraquat in the blood made also possible to determine the Paraquat intoxication severity score, multiplying the initial concentration of Paraquat (µg/mL) over the time (hours) occurred after ingestion and until the treatment.

If above 50, it is an early death due to circulatory

failure; between 10 and 50 the death is later, due to respiratory failure; if it is lower than 10 survival is possible.[5] It is important to highlight that this score uses the Paraquat concentration in the serum and not in the plasma (where more usually the dosage to be done), and this can lead to some difficulties in construing the results, once that in the serum the concentration is around three times lower. [5] There are studies pointing to the predictive curb in Proudfoot's nomogram, subsequently adapted by Hart, and it is more precise in determining the prognosis than the Paraquat intoxication severity score. [5]

More recently, it was proposed by Huang et al (2003, 2006),[15,16] the use of the APACHE II system (Acute Physiology and Chronic Health Evaluation) [17] to assess the severity of Paraquat intoxications. In one of those studies (n= 58) it was verified that APACHE II values equal or above 20, were associated to a higher intra-hospital mortality rate. [15] In another study (n= 64) it was demonstrated that APACHE II system values above 13 would predict hospital mortality, with a sensitivity of 67% and specificity of 94%. [16] However it is important to mention that this score rate was validated in the Intensive Care Unit, with data got in the first 24 hours of admission. Such fact would make difficult to apply this system in the case of Paraquat intoxication with later toxicity, where many times the low initial value in the APACHE does not invalidate a bad prognosis, and the subsequent individual death.

There are studies considering some analytical results, determined when the patient is admitted in the Emergency Service, determinant to the prognosis. It was verified that leukocytosis, creatinine, urea nitrogen, hepatic enzymes, amylase and glucose increases are more marked in patients with worst prognosis.[5]

In spite of the importance of Paraquat in the blood, it can be seen that most hospitals in Portugal do not have access to this result within a reasonable timeframe, and they keep on using Paraquat urine test, in spite of the high number of untraceable false results. Moreover, often the fact Paraquat in the urine is untraceable leads to suspending the treatment, and this can make the prognosis worst. Therefore it should be performed early on, detecting Paraquat in the urine keeping the treatment while doubts on the diagnosis persist,[11] or until severe side effects from the therapy emerge. Meanwhile it should be reached, as soon as possible, the Paraquat value in the blood to confirm the diagnosis. If this is not possible therapy should be kept, associated to a clinical and analytical tight monitoring, in the sense of controlling the appearance of possible side effects of Paraquat intoxication which would confirm the diagnosis. In conclusion the decision of starting, keeping or suspending the therapy is very complex and should be tailor-made for the individual, valuing his/her clinical history and evolution.

## TREATMENT

The treatment has three objectives: to prevent or to reduce absorption, to promote Paraquat quick excretion and to modify tissue effects.

To prevent absorption is the most important stage of the treatment,[3] and a nasogastric probe should be place in order to have a gastric washing with 3 to 5 L of saline solution,[1,6] and adding activated carbon (1 g/kg), or Fuller's earth (300 g of solution 30%) and magnesium sulphate (250 mg/kg); these should be removed after 20 to 30 min and administered again every 3 to 4 hours, for 48 hours.[3]

A good hydration, by endovenous and oral route should be made to promote diuresis. In the presence of erosions in the oropharynx or the esophagus. the patient must remain in zero diet and with analgesia, being hydration ensured through endovenous route.[4]

Oxygen should not be administered, because it worsens toxicity induced by Paraquat while favoring the formation of free radicals, and can increase mortality.[7] It can only be used in cases of severe respiratory failure.[3,4]

Paraquat quick excretion is recommended, although its clinical value is arguable whatever technique is used. One of the methods proposed is forced diuresis, a simple technique of immediate use, enabling Paraquat maximum clearance in the first 24 hours, when there is not an acute renal insufficiency with a renal elimination 2 to 10 times above hemocarboperfusion.[1] While performing such procedure, the diuresis should be kept at least at 200 mL/hour using for such purpose high doses of furosemide. However this has stopped to be recommended, as it reduces the efficacy removing Paraquat from the body after the first day of intoxication.[3,4]

Hemocarboperfusion consists of an extra-corporal circuit with an absorbent particles set, usually of activated carbon, where the blood is filtered. [4] It is effective extracting most toxic substances, except

heavy metals and carbon monoxide. In the Paraquat intoxication its efficacy is limited and controversial, [3] once that it is stored in the intracellular compartment due to its high lipid solubility and/or binding capacity to the tissues. Therefore, to reduce tissue reserves it is necessary to perform hemocarboperfusion in a sustainable and prolonged way.[3] Main complications are hemorrhages, arterial hypertension and hemoglobin, platelets and serum calcium decrease.[3] There are studies which indicate the existence of benefits using hemocarboperfusion in the first 12 hours (preferably in the first 4 hours) in individuals with survival probability between 20 to 70%, according Hart's nomogram. [1,4,18,19] However when the doses are higher than lethal ones, the prognosis is highly reserved, such procedure seems useless, it does not reduce mortality, in spite of reducing the intoxication severity and increasing the survival time.[4,19] Also in this case, to test the blood for Paraquat is important to ascertain the probability of survival and subsequently the hemocarboperfusion usefulness. In spite of all, there are studies proposing continuous hemocarboperfusion to prolong life until other therapies are possible, namely pulmonary transplant.[4]

Haemodialysis may have some efficacy when serum Paraquat concentrations are high, although its efficacy is lower than the hemocarboperfusion, [1,20] because Paraquat is not appropriately dialysable, once it has a high volume of distribution, mainly intercellular and high molecular weight.[3] Besides, as forced diuresis, this technique efficacy removing Paraquat decreases after 24 hours of its ingestion.

Plasmapheresis has a clearance capacity similar to hemocarboperfusion,[4] without some of its disadvantages, namely make useless the adsorption filter as thrombi are formed, loss of blood cells and the need for anticoagulation.[3]

Several drugs have been proposed as modifiers of Paraquat tissue effects, absorbed but not excreted, with a very doubtful efficacy. The most used with some antioxidant effect are the desferrioxamine, seeming to reduce the pulmonary lesion and the N--acetylcysteine, with beneficial effects in liver toxicity. Vitamin E is less used, because it does not change either acute mortality or pulmonary pathophysiologic changes on the long-term.[6, 21] Ascorbic acid does not have a benefit demonstrated in vivo.[1]

The association of immunosuppressant therapy (cyclophosphamide) with corticosteroids, namely methylprednisolone, can be useful, but there is no consensus on this respect.[3] Methylprednisolone, in high doses, seems to have some effect in reducing mortality in moderate to severe intoxication, once it interferes in lipid metabolism blocking phosphatases in the cell membrane, preventing peroxidation and cell destruction.[6,22] Such effect seems to be potentiated when cyclosphosphamide is associated, a wide spectrum immunomodulator, influencing virtually all the cellular and humoral components of the immune response.[23] A high-dose of cyclophosphamide can cause leukopenia, in one to two weeks and reducing the severity of inflammation in such patients.[23] According to a study by Lin JL et al.,[23] using metal methylprednisolone pulses for three days and cyclophosphamide for two days, associated to the prolonged use of dexamethasone, can be effective for individuals intoxicated with Paraquat.[23]

The use of two different steroids is related with the fact of dexamethasone pulses use to be associated with toxicity, opting by its prolonged use after methylprednisolone pulse, because it is more potent than the same dose of methylprednisolone [24] and cheaper.

To use anti-Paraquat antibodies is not useful, once that in vitro they sequestered Paraquat in the plasma, without avoiding its accumulation in the tissues, increasing inclusively its fixation on the liver.[1,25]

The efficacy of all these substances is very arguable and in spite of all efforts, the only certainty that we have at present is that when taken high doses of Paraquat, there is not an effective treatment.

Over the years many protocols have been proposed. In 1984, Addo and Poon King[1,25] carried out a study including 72 patients intoxicated with Paraquat which were treated in the following way: general procedures and dexamethasone, 8 mg, every eight hours, endovenous route for two weeks; afterwards dexamethasone, 0.5 mg every eight hours, oral route, more two weeks and cyclophosphamide, 5 mg/kg, every eight hours for two weeks up to a maximum of 4 g. None of the patients has undergone hemocarboperfusion. The survival rate in this group was of 72%, while in the control group, subject only to general measures was of 28%.[1,25] However in 1992, another similar trial with 47 patients was carried out without evidence of treatment advantage regarding the control.[27]

Lin,[22] in 1995, has carried out a study with two groups undergoing hemocarboperfusion for 8 hours,

**TABLE I**

**Therapy protocol in Paraquat poisoning**

- Do not administer oxygen, except if there is a severe hypoxemia (PaO2 < 40 mm Hg);
- Diet 0 (if there are erosions on the oropharynx and esophagus);
- Placing a nasogastric probe, if there is a suspicion of caustic lesion in the digestive tube;
- Gastric lavage with 3 to 5L of saline solution;
- Activated carbon (1g/Kg) or Fuller's earth (300g solution at 30%) and magnesium sulphate (250 mg/Kg) administration, to be removed after 20 to 30 minutes and repeated every 3 or 4 hours, for 48 hours;
- Analgesia and abundant fluid therapy by endovenous route;
- Furosemide IV to obtain a 200 mL/h diuresis;
- Hemocarboperfusion (6-8 hours),to be kept at least until the urine test for Paraquat result is known;
- Cyclophosphamide, 15 mg/kg diluted in 100 ml dextrose at 5%, to be infused in 60 minutes, once a day, for two days (after the hemocarboperfusion first session);
- Methylprednisolone, 15 mg/kg diluted in 200 mL dextrose at 5%, to be infused for 60 minutes, once a day for three days (always after a hemocarboperfusion);
- Desferrioxamine, 100 mg/Kg, diluted in 500 ml dextrose at 5%, in continuous infusion for 24 hours at 21 mL/h (after the first hemocarboperfusion session);
- N-acetylcysteine, 150 mg/kg diluted in 500 mL dextrose at 5%, to be infused for 3 hours (after desferrioxamine infusion), followed by 300 mg /kg diluted in 500 mL dextrose at 5%, in continuous infusion at 21 mL/h, for three weeks;
- Dexamethasone, 5mg, endovenous, every 8 hours, after methylprednisolone suspension up to the 3rd day, until PaO2> 80 mm Hg;
- Preventing stress ulcer (omeprazole 40 mg endovenous, twice a day).

in the first 24 hours and, in one of them with 17 patients were carried out only general procedures, while in the other, with 16 patients was administered methylprednisolone pulse1 g/day, for three days and cyclophosphamide, 1 g per day, for two days. The group survival subject to conventional therapy, without pulses, was of 29.4% being of 72% in the group subject to methylprednisolone and cyclophosphamide pulses.[22]

Bottela and Maglia et al. [28] carried out a study in 29 individuals who have ingested a lower dose than 45 mL, verifying that the use of dexamethasone, 8 mg, every 8 hours, endovenous route, for two weeks, followed by 0.5 mg, every 8 hours, endovenous route, a further two weeks, and still furosemide 5 mg/kg, every eight hours, endovenous route, two weeks, and still furosemide and vitamin B and C in high doses, was associated to a lower mortality.[1,25]

According to some works published, the therapy described in Table 1, when applied precociously seems to be effective in the treatment of individuals who have ingested small quantities of Paraquat. Unfortunately such protocol has not shown to be effective when applied at a later stage or when lethal doses are ingested.[2-5]

In spite of such protocol seeming until now the most adequate, there is a study published in September 2009 by Ricardo Dinis-Oliveira not confirming its efficacy.[2] In this work tissues of five patients who died due to Paraquat intoxication, subject to therapy protocol similar to that described previously were assessed. The histologic result has revealed that the drugs administered were not capable of preventing the accumulation of lethal doses in the tissues, nor even important structural changes.[2] At pulmonary level, apart of an intensive vascular congestion, signs of diffuse intra-alveolar clotting suggests the use of anti-thrombotic drugs in the treatment of intoxication by Paraquat with the objective of preventing the intravascular and intra-alveolar coagulation. [2] Besides were detected for the first time, deposits of anthracosis pigments in the walls of the great vessels and in the cytoplasm of cells similar to alveolar macrophages. All patients were living in semi-urban areas and were not smokers, therefore such authors raise the hypothesis of such carbon deposits being secondary to adsorbent particles sets of activated charcoal, used in hemocarboperfusion, representing a possible adverse effect of such technique. [2] In this study, as in others, [4,29] hemocarboperfusion was not capable of removing totally Paraquat from the patient's organism, even in the case of the one who survived six days and was subject to 7 sessions of hemocarboperfusion lasting eight hours each.[2] In the study carried out by Rui Castro et al., where 24 patients were included, the use of hemocarboperfusion did not help reducing mortality. However when used at a very early stage, hemocarboperfusion increases effectively the Paraquat elimination. [2]

Meanwhile other therapeutic options have emer-

ged, applied in sporadic cases, as pulmonary radiotherapy[30-35] in individuals with irreversible pulmonary fibrosis at the end of one year, or pulmonary transplant,[36-37] with very contradictory results.

In a study carried out in rats, with administration of thalidomide (acting on TNF anti-ARNm) associated to montelukast (competitive inhibitor of cysteinyl-leukotriene receptors) and acetylsalicylic acid, was verified a reduction on pneumocytes destruction and fibroblasts proliferation in highly vascularised areas, reducing pulmonary fibrosis, probably due to the anti-fibrinogenic and anti-inflammatory action of such drugs. [38]

Other therapies seems to be promising in animal studies : propofol, increasing average survival time of Paraquat intoxicated rats, due its capacity of removing free radicals; sodium salicylate, seeming to have a beneficial effect in rats pulmonary lesions, inhibiting the activation of pro-inflammatory factors, the platelet aggregation, oxidative stress, collagen deposition, disruption of clear cells and pneumocytes type I and II, pulmonary edema, lipid peroxidation, protein oxidation and ADN fragmentation. [5]

Due to the severity of the clinical situation it is necessary the permanent monitoring of such patients, reason why they should be monitored in an intensive care unit or at least an intermediary one where there are material and human appropriate resources. Organ support therapy, namely hemocarboperfusion should be kept while it is beneficial for the patient, and should be suspended if there are severe side-effects refractory to therapy as hemorrhage, severe hypertension, thrombocytopenia and/or anemia. Mechanical ventilation should be implemented in cases is young patients and without severe co-morbidities, if it is predicted a possible pulmonary transplant on the short term. Prognosis of patients in need of keeping such support therapies is not good, and it should be reserved only for cases where according Hart's nomogram there is a probability of survival. When Paraquat intoxicated individuals do not respond to the implemented therapy, and their general condition is deteriorating; when according to Hart's nomogram, the probability of survival is minimal or when are elderly with multiple comorbidities, without conditions to overcome such aggressive therapies, there should be implemented only comfort procedures.

## CONCLUSION

Paraquat intoxication is a very complex situation, in most cases fatal. Before a case suspected of intoxication, blood tests to trace Paraquat should be carried out, without conditioning the therapy only to Paraquat urine values. There is not an effective therapy when high quantities of Paraquat are ingested. It is important an investment searching for new treatments, on inspections and penalties on the sale of such herbicide, with the aim of keeping its trade forbidden. If there is ingestion, it seems recommended to use the therapeutic protocol described in the text, because when it is applied at an early stage, it has a positive impact on the survival of patients who ingested small quantities of Paraquat. ■

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