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A) COMMENTS ON PUBLISHED ARTICLES

Comment on "Acute renal failure after intake of mushrooms"

Nefrología 2009;29**(6)**:608.

Dear Editor,

After carefully reading the article by Rojas et al (*Nefrología* 2008;28[5]:559-560),[1] we would like to make a series of observations which we believe should be taken into account. The article describes the case of a child who, after consuming wild mushrooms, had symptoms of vomiting without the presence of diarrhoea, followed by anuric renal failure, anaemia and mild hepatic cytolysis, and needed haemodialysis for 8 days with satisfactory progress.

While discussing the case, the article mentions hepatotoxic mushrooms carrying amatoxins as the cause of the illness. However, in our opinion, the absence of diarrhoea, present in 100% of such poisoning,[2] together with the mild hepatic cytolysis and the normal prothrombin time, render the involvement of a hepatotoxic mushroom such as *Amanita verna* highly unlikely.

The erroneous use of the references is surprising. Five of the six articles mention poisoning from mushrooms of the *Cortinarius* genus, the symptoms of which greatly differ from those described here. The digestive symptoms indicate a latency of 3 days in appearance and renal failure of 4 to 15 days, leading to chronic kidney disease (CKD) in 34% of the cases without hepatic affectation in all the cases shown.[3]

However, the case described by Rojas et al is of particular interest because it corresponded to many of the data attributed to an accelerated nephrotoxic syndrome caused by mushrooms, which is described as being caused in the USA[4] by the *Amanita smithiana*, in Japan by the *Amanita pseudoporphyria* and in France,[5,6] Italy and Spain[7] by the *Amanita proxima*. The latter, that is, *Amanita proxima* (Dumée, 1916), is a mushroom with a creamy white colour similar to *Amanita ponderosa* or *Amanita ovoidea*, with which it is usually confused. It has an orange volva that is characteristically different from the rest of the white-coloured fungi, and it is predominantly found in the Mediterranean area.[5,6] De Haro et al,[5] with the greatest amount of cases (53 patients), report that between 2 and 48 hours following post-ingestion all patients showed signs of gastroenteritis, with a high number of vomiting (85%) and a lesser amount of diarrhoea (26%). Leray et al,[6] in a smaller amount of cases, report no diarrhoea. Acute renal failure occurred between days one and four following ingestion, always accompanied by mild cytolysis that was quickly reversible with a prevalence of LDH and GPT/ALT, the latter never surpassing 15 times the maximum normal limit. Renal affectation is histopathologically characterised by acute tubulointerstitial nephritis with an always-favourable progress.[6] The toxin responsible has yet to be isolated; however, suggestions have been made of non-protein amino acids, thermo-stable and similar to those found in other nephrotoxic fungi, for example, allenic norleucine isolated in the *Amanita smithiana*.[4]

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B) BRIEF PAPERS ABOUT RESEARCH AND CLINICAL EXPERIENCES

Continuous extrarenal treatment without anticoagulation therapy

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Dear Editor,

Critically ill patients often develop acute renal failure and, on many occasions, need continuous extrarenal treatment. One of the main disadvantages of the technique is the coagulation of the filters, which reduces the effectiveness of the therapy, increases costs and prolongs the patient's recovery. The continuous nature of the technique, therefore,

requires an anticoagulation system to guarantee its effectiveness, optimise the survival of the circuit and reduce blood loss due to filter coagulation.[1] However, this will increase the risk of haemorrhage already run by these patients. Furthermore, turbulent blood flow and interaction of the membrane with platelets could induce platelet dysfunction, which increases the risk of haemorrhage.[2] The objective is to keep the filter, the extracorporeal lines and the catheters free of clots, avoiding a systemic anticoagulation that favours haemorrhage complications. The need for anticoagulants will depend on technical factors, such as the applied blood flow or the type of the filter membrane, as well as on patient-related factors, namely the hepatic function and the number of platelets. It is important to understand the intrinsic mechanisms involved in the premature coagulation of the filter's circuit to optimise anticoagulation and keep the filter from coagulating for the longest amount of time possible. Many studies have been carried out, one by Tank et al,[3] which shows that continuous extrarenal treatment in critically ill patients at a high risk of haemorrhage can be performed without anticoagulation, which minimises the risk of haemorrhage and it is linked with an acceptable filter lifetime.

The objective of our study is to examine the lifetime of the filters used in techniques of continuous renal treatment, with or without anticoagulation, for critically ill patients with or without coagulopathy. For this reason, a prospective, cohort study was carried out in a polyvalent intensive care unit of a third-level hospital for a period of four months. Patients at a high risk of haemorrhage were included, i.e. those who suffered from active bleeding or had an episode of major bleeding during the last 48 hours, the 24 hours post operation or those who had a Quick index of < 50% and/or aPTT of > 60 seconds and/or a platelet count of < 60,000/ml. The Prisma system was used on all the patients with predilution replacement, which was present in patients with renal failure (acute or chronic) and haemodynamic instability, requiring liquids management and controlling electrolytes or the acid-base equilibrium. The mean time (mt), counted in hours, of the filters and their standard deviation were analysed as statistical data by comparing the average values by means of the Fisher test.

Twelve patients took part in the study, 8 men (66%) and 4 women (33%), with APACHE II and SAPS scorings of 17 and 35, respectively, when admitted to hospital. Forty-eight filters were analysed, of which 28 (58.3%) corresponded to patients at a high risk of haemorrhage, with an mt of 21.8 ± 4.09 hours. Heparin was administered intravenously in 12 filters (25%) at an anticoagulant dose, with a filter mt of 17 ± 6.5 hours. Finally, in the 8 filters (16.6%) corresponding to the patients without any risk of haemorrhage, who were only administered subcutaneously a prophylactic dose of heparin against deep vein thrombosis, the mt was 16 ± 4.2 hours.

When comparing the average lifetime of the filters in patients without any risk of haemorrhage, there are no significant differences between those who were administered heparin intravenously at an anticoagulant dose and those who only received prophylactic heparin subcutaneously ($p = 0.70$). As expected, the mt of the filters in patients with coagulopathy is significantly greater than those administered intravenous heparin ($p < 0.05$) or those who received the prophylaxis dose ($p < 0.01$).

The ideal anticoagulant would prevent coagulation of the filters without causing haemorrhage, would have a short half-life with an action limited to the extracorporeal circuit and easy monitoring, secondary effects would not exist and it would provide an effective antagonist. None of the currently available anticoagulants can satisfy all these prerequisites. The most commonly used method to prevent coagulation of the system is the continuous administration of heparin in the proximal line of the extracorporeal circuit. Patients at risk have been recommended heparins of a low molecular weight, prostacyclins, regional heparinisation with protein neutralisation, regional anticoagulation with citrate, prostacyclins and the infusion of predilution saline solution.

To conclude, the replacement administered before the filter dilutes the filter's blood reduces haemoconcentration and improves rheological conditions. Its use is suitable when the platelet count is < 60,000/ml, the APTT is > 60 seconds or twice the control value, the INR is > 2 or when there is spontaneous haemorrhage or a disseminated intravascular coagulopathy. Recent studies show that critically ill patients at a high risk of haemorrhage, and undergoing these continuous therapies, can be treated without anticoagulation of the circuit, thus without altering the circuit's half-life.[4,5] In our study, in which we used predilution replacement, we can confirm that the filters of the patients without any risk of haemorrhage have the same half-life whether or not they anticoagulate. These results need to be confirmed with studies of a greater sample size.

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