The nephrologist as a consultant for acute poisoning: epidemiology of severe poisonings in the state of Rio Grande do Sul and techniques to enhance renal elimination

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Abstract

Accidental and intentional poisonings or drug overdoses constitute a significant cause of aggregate morbidity and mortality, and health care expenditures. The nephrologist is frequently called to the emergency room and ICU as a consultant to help with the indication of measures to enhance renal depuration of toxic agents. This study reviews the use of dialysis in acute poisonings due to medications or pesticides, whose specialized toxicological support was provided via telephone by the Poison Control Center of the state of Rio Grande do Sul. The correlation between need for dialysis and death was assessed in a retrospective cohort (1998-2000). Of the 36,055 cases registered, 337 were identified as severe, and 245 met the inclusion criteria required. Mean age was 30 ± 18 years, and 53% of the patients were women. The most commonly involved medications were anticonvulsants and antidepressants, and the pesticides were organophosphates, bipyridyl compounds, and glyphosate. Techniques to enhance elimination included urinary alkalinization (n = 37) and dialysis. In severe poisonings, dialysis was performed in 4.5% of the cases (n = 11), 3.67 procedures/year (1/22.7 reports of severe cases). In the group undergoing dialysis, 91% involved a suicide attempt (mainly phenobarbital and paraquat). Two cases required hemoperfusion (chloramphenicol and paraquat). Death among non-dialyzed severely ill patients occurred in 25.6%, *versus* 36.3% of dialyzed patients (RR = 0.89; 95% CI = 0.54-1.35). The findings can be explained by the statistic power associated with the number of procedures performed. The nephrologist should be aware of situations requiring the use of dialysis, even if not necessarily aimed at renal replacement, but at enhancing depuration of a toxic agent.

Keywords: toxicology, dialysis, hemoperfusion, poisoning.

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Introduction

Accidental or intentional poisonings, as well as drug overdose, constitute a significant cause of aggregate morbidity and mortality and health care expenditure.[1] Currently, approximately 2.3 million events involving poisonings and drug overdoses are estimated to have occurred in the United States of America in the year 2000.[2] In 2008, the American Association of Poison Control Centers (AAPCC) recorded almost five million notifications, but the confirmed number of poisoning accidents involving human beings has practically remained unaltered (2.4 million).[3] In Brazil, the National Poison Control System (SINITOX) recorded in 1999 slightly over 66,000 cases of human poisoning,[4] and the last survey published using 2007 data reached almost 120,000 cases.[5] For both situations, with a greater emphasis on the Brazilian scenario, the actual incidence is still unknown, because of the lack of adequate diagnosis and under-notification.[1-5]

Acute accidents of unfavorable outcome can require measures to increase renal excretion, such as dialysis, to remove waste products.[6] In certain cases, acute kidney failure secondary to poisoning can be determinant for dialysis indication. Only a few studies have shown that methods that enhance elimination actually shorten the duration of poisoning clinical findings or improve clinical outcomes.[2,3,7]

In 2008, the following methods to enhance elimination were prescribed in the USA and the figures have varied only slightly as compared with data from the year 2000: urinary alkalinization in 9,602 accidents; hemodialysis (HD) in 2,177 cases; hemoperfusion (HP) in 27 cases; and other extracorporeal procedures, such as HP and hemofiltration (HF), in 31 events.[2,3] A historical data review from the Toxic Exposure Surveillance System (TESS) recorded by the AAPCC has shown that, while extracorporeal dialysis methods for managing poisoning have been increasingly indicated over the past decades (a six-fold increase from 1986 to 2004), peritoneal dialysis, which represented up to one fifth of the indications in the mid 1980s, has no longer been prescribed for that purpose since 2001.[8]

Although uniform data systems for poison centers (such as TESS) have existed in the USA since 1985, real-time toxicovigilance began only in 2003.[2,7] Computed-based systems are essential for maintaining quality records. Pioneering initiatives, such as telephone record and support, provided by Poison Control Centers have existed in Brazil for at least three decades, one example being the Poison Control Center of the state of Rio Grande do Sul (1976).[1] In 1980, the Health Ministry constituted the SINITOX, affiliated to the Oswaldo Cruz Foundation, which, since 1985, has annually reported cases of human poisoning of the 37 Poison Control Centers currently existing in our country.[9]

Considering the scarce literature on the topic, methods for enhancing renal elimination in our country are not well known. In addition, population surveys are required to provide a sufficiently large sample to allow valid conclusions. However, the identification of such severe, although rare, events requires that nephrologists be up-to-date with the management of situations for which they are consulted, at both emergency and intensive care units (ICUs).

Objectives

This study aimed at the following: to determine the incidence of the use of dialysis methods to manage severe poisonings due to drugs or pesticides of agricultural use at a regional referral center for poisonings; to assess whether dialysis methods were effectively used when indicated; and to discuss the relation between the need for dialysis and poisoning outcome.

Material and Method

Outline

This is a historical cohort study with non-conditioned population sampling. Incidence endpoints, whose major therapeutic intervention of interest consisted in verifying the performance of dialysis for poisoning management, were considered. The report cards of acute poisonings registered in the Poison Control Center of the state of Rio Grande do Sul, an agency affiliated to the Health Secretariat of the state of Rio Grande do Sul, from 1998 to 2000 were reviewed. According to the SINITOX data, the two categories of toxic agents accounting for the greatest absolute number of deaths due to human poisoning in Brazil in 1999 were medications and agricultural poisons. Metals were not included, because they were commonly involved in cases of poisoning secondary to chronic exposure. Accidents involving poisonous animals were not studied. The sample of cases to be reviewed comprised those defined as severe by the toxicologist in charge at the time of assistance. On that occasion, the cases were followed up until definition of hospital discharge or death. The presence of at least two objective criteria was required to define a severe case. The objective criteria used to meet that category of severity were as follows: the extremes of the age range (children and elderly); the type of chemical agent involved; signs or symptoms over the course of the poison event (such as coma, convulsions, need for ICU admission, use of ventilatory support); and outcome of the accident. The following cases were excluded from the study: cases referred as severe, but that did not meet the above cited criteria of severity; cases whose outcomes were not confirmed (cure, sequela, or death); unknown age or chemicals; and deaths due to circumstances not directly related to poisoning.

Statistical analysis

Data were compiled by use of the software Microsoft ® Access 2000, version 9.0.2812, and statistical analysis was performed with the software Statistical Package for Social *Science (SPSS®)*, version 10.0.1, 1999. The statistical tests used were as follows: two-tailed *t* test for continuous variables; and Pearson chi-square test or two-tailed Fisher exact test for categorical variables. The maximum alpha error admitted was 5% ($p < 0.05$). The study was submitted to and approved by the Committee of Ethics of the institution. Financing and conflict of interest do not exist.

Results

Of all cases registered at the Poison Control Center of the state of Rio Grande do Sul during the period studied (46,094), those of effective human poisoning (mild, moderate, or severe) comprised 36,055, from which all cases defined as severe and secondary to medications or agricultural poisons (n = 337) were selected. After applying the inclusion and exclusion criteria, 245 cases were left.

Descriptive analysis and incidences

The cases of severe acute poisoning studied (n = 245) showed a slight predominance of the female sex (53.1%). The mean age of the group was 30.6 ± 18.3 years, and was similar for both sexes (men, 31.3 ± 17.3 years; women, 29.9 ± 19.2 years; p = 0.08).

Medications were the chemicals most frequently involved in acute accidents (65.3%; Figure 1), and comprised mainly anticonvulsant drugs, antidepressants, barbiturates, sedatives, and antipsychotics. Pesticides (36.3%) comprised organophosphates, bipyridyl compounds (paraquat and diquat), and glyphosate (Figure 2). Illicit drugs (in isolation or in association with other compounds) were identified in 10.2% of the accidents. The context was suicide attempt in 80.4%, and individual accidents accounted for only 9.4%. The large majority (79.6%) of cases occurred in urban areas. The preferential via of poisoning (94.7%) was the oral one.

Regarding the decontamination measures used, spontaneous vomiting occurred in 7.8% of the accidents. Vomiting induction, either mechanical or with ipecac syrup, was not indicated to any patient. Gastric lavage was performed in 72.7% of the cases and activated charcoal was used in 69%. Saline cathartic was indicated in 23.3%, but its effective use could not be confirmed in all cases. In 40.4% of the accidents, at least one antidote was proposed and effectively used for managing acute poisoning.

Some severe poisoning cases have also undergone methods for enhancing excretion. Urinary alkalinization was performed in 18.4% of the cases. Hemodialysis was indicated in 30 accidents (12.2%), but performed only in 11 (4.5%). Charcoal HP was reported in two accidents (involving chloramphenicol and paraquat), but in association with HD. The use of the following methods was not reported: peritoneal dialysis; HF; exchange transfusion; plasmapheresis; and total intestinal irrigation.

Data regarding ICU admission and use of mechanical ventilation (MV) were collected essentially to establish the severity of the accidents. In 197 cases (80.4%), ICU support was required, and 125 patients (51%) needed MV at some point during hospitalization.

Toxicological analysis was not performed in the majority of severe accidents (79.2%). When performed, it involved quantitative (12.7%) and qualitative (2%) laboratory measurements. Toxicology screening

Figure 1. Major categories of agents involved in severe acute poisonings.

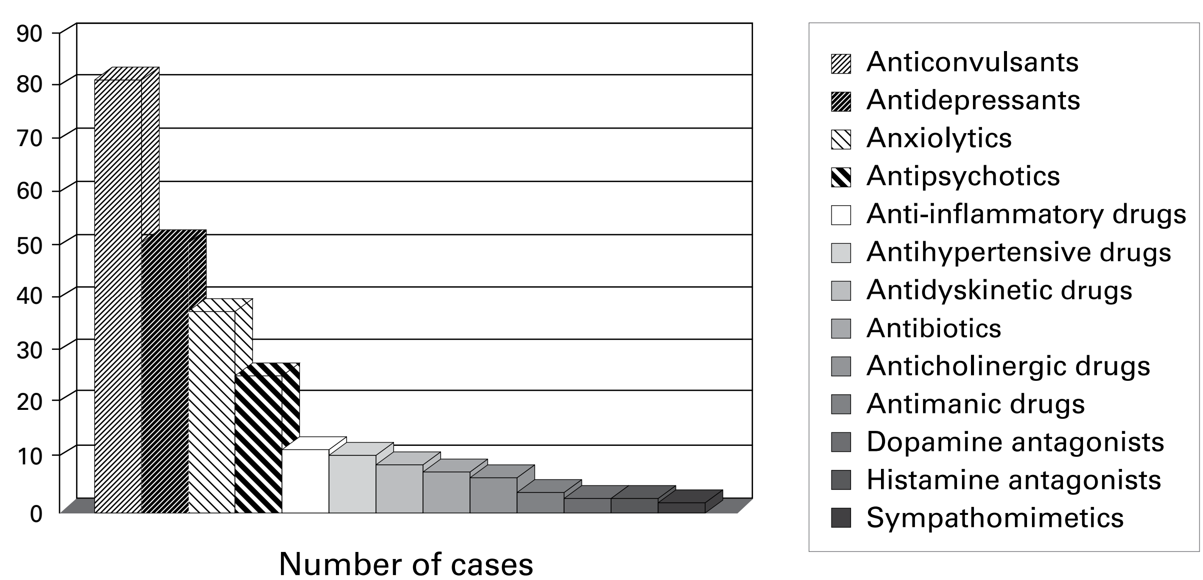
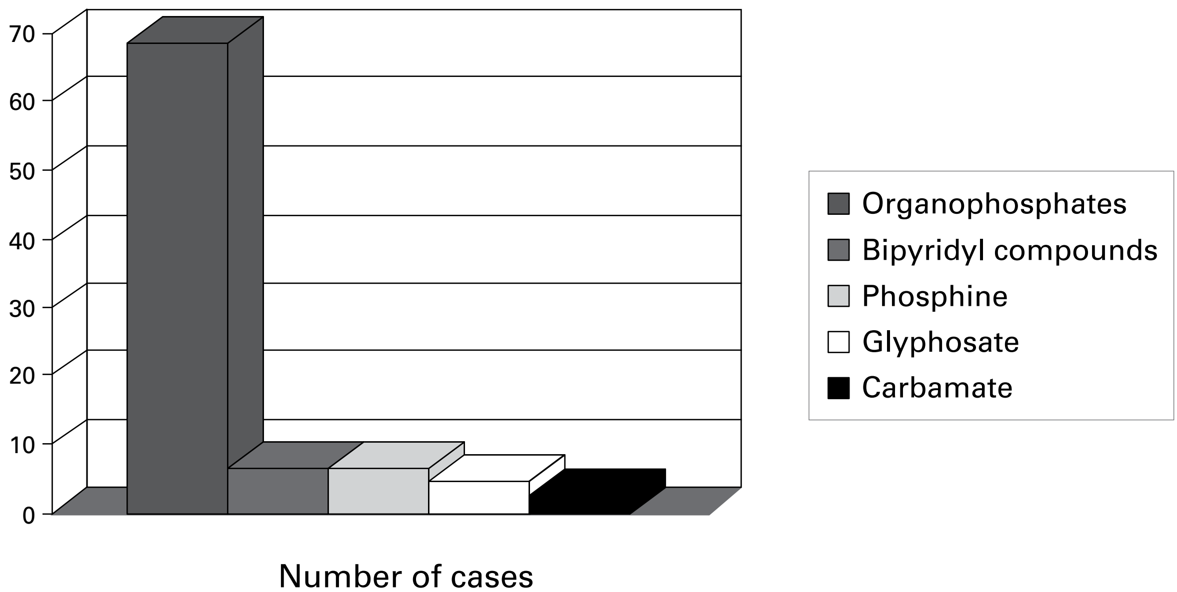


Figure 2. Major agricultural poisons involved in severe accidents.



in isolation was performed in 2.9% of the cases, and in association with the quantitative analysis of the agent identified in the screening itself, in 3.3% of the cases.

Outcome of severe accidents

The general incidence of deaths was 26.1% (64 cases). The mean age of the patients who died was 38.8 ± 18.9 years, and that of patients surviving poisoning was 27.6 ± 17.2 years (p = 0.0001).

Relationship between variables

An association was observed between death and the following variables: male sex (p = 0.009); rural area (p = 0.0001); agricultural poison use (p = 0.001); and suicide attempt (p = 0.042). No association was observed between illicit drug use and death (p = 0.09).

No relation was evidenced between the use of gastric lavage or of antidotes in poisoning management and death (reduction) (p = 0.254 and 0.128, respectively). On the other hand, the use of activated charcoal and urinary alkalinization associated with a reduction in death (p = 0.01 and p = 0.001, respectively).

A relation between ICU admission and patient's death was observed; being at the ICU is a limiting factor to the number of deaths (p = 0.006), but requiring or not ventilatory support seemed not to modify the outcome in question (p = 0.695), since the percentage of deaths in the groups undergoing or not MV, as well as the number of patients in the groups, was similar.

Dialysis use

Eleven patients received extracorporeal measures for enhancing elimination of the toxic agent. Most of them (n = 10) underwent HD, and only one patient received HP. Of those 11 accidents, ten were due to suicide attempt (five with medications and five with agricultural poisons). Only one medicamentous poisoning was reported as accidental (supratherapeutic dose).

Phenobarbital was the agent involved in suicide attempt, and, in one of such cases, lithium and two tricyclic antidepressants were associated. In accidents involving agricultural poisons, bipyridyl compounds were the agents used (four cases of paraquat and one of diquat). The only case not related to suicide attempt consisted in prescribing and administering a supratherapeutic dose of chloramphenicol to a child. In all cases, there was indication for HD, but, in five, HD maintenance was required because of the development of acute kidney failure secondary to poisoning.

Of the 11 patients undergoing HD or HP, four died (36.3%), a greater percentage of death than that of non-dialyzed patients (25.6%, n = 234), but that difference was not significant as a relative risk factor (RR = 0.89; 95% CI = 0.54-1.35).

Potential indication of dialysis treatment

The 245 poison accidents studied were classified according to the possibility of dialysis use, aiming at removing drugs and chemicals. Considering exclusively the type of chemical agent involved, of those studied, 185 had a possible theoretical indication of dialysis or HP. Both procedures (HD and/or HP) were indicated in 102 cases; only HD in 20 cases; only HP in 63 cases. The incidence of death in all cases with any indication of dialysis (n = 185) was 24.8% (46 deaths, $p < 0.05$; 95% CI = 18.6%-31%). Of the cases with no theoretical indication for dialysis (n = 60), the incidence of death was 30% (18 deaths; $p < 0.05$; 95% CI = 18.5%-41.5%).

In the cases with effective dialysis recommendation by a toxicologist in the report card of the patient (n = 30), the incidence of death was 9 cases (30%; $p < 0.05$; 95% CI = 13.6%-46.4%).

Discussion

The general management of the poisoned patient consists mainly in an appropriate assessment, with recognition of the occurrence of poisoning, followed by suspicion and identification of the agent(s) involved and determination of the severity by estimation of toxicity. The treatment consists of essential symptomatic and supportive care, followed by the attempt to reduce the absorption of the toxic agent, which may require the administration of antidotes and/or enhancement of the elimination of the agent that has already been absorbed.[6,8,9,10]

Decontamination measures are not always sufficient and/or necessary for managing certain poisonings. Antidotes and methods to enhance elimination then become necessary. Situations with indications for techniques to enhance elimination include the following: poisoning with a substance whose elimination is known to be increased by use of a certain technique; lack of patient's response to the support medical care used; nature of the toxins; poor endogenous clearance; associated diseases or comorbidities that predict a complicated clinical course; and situations in which the benefit obtained with a certain intervention exceeds the risk of complications inherent to the procedure.[11] The available elimination methods consist of the following: use of multiple doses of activated charcoal; saline diuresis; urinary alkalinization or acidification; extracorporeal methods (HD, HP, peritoneal dialysis, HF, plasmapheresis, and exchange transfusion); hyperbaric oxygen; chelation; removal of cerebrospinal fluid; and immunotherapy (specific antibodies against toxins).[6,8,11,12]

As only a few studies have described changes in clinical outcomes when elimination techniques are used, the primary assessment has been based on pharmacokinetic benefits. Each technique is associated with potential complications, and its choice should be based on the type of drug ingested, current prognosis and poisoning potential, presence of contraindications, and efficiency of alternative methods.[2,3,6,7,9]

Techniques to enhance elimination have been used in approximately 1% of the exposures in the USA.[3,7] They can accelerate toxin removal, but few studies have investigated the extent to which they actually shorten the clinical duration of poisoning or enhance clinical outcomes.[6,11]

The objective of urinary alkalinization is to achieve a urinary pH equal to or greater than 7.5, usually associated with a urinary volume greater than 3 mL/kg/hour (adults). After undergoing glomerular filtration, a drug with a weak acid character is more easily eliminated in the presence of a pH increase in tubular lumen, because of the increase in the proportion of drug in its dissociated form (in its constituent ions), which, by altering its characteristics of tubular liposolubility, impairs resorption and increases excretion.[11,13,14] In the present study, accidents involving phenobarbital are worth noting, because of the important and persistent central nervous system depression they cause and the frequency with which they are associated with severe suicide attempts. Urinary alkalinization was used in 37 accidents, 97% of which (n = 36) involved phenobarbital (as an isolated causal agent in 21 cases, and in combination with other agents in 15 cases). The other poisoning in which alkalinization was used involved acetylsalicylic acid (one case). Use of sodium bicarbonate solutions aimed at serum alkalinization (cardioprotective effect against severe arrhythmias), and not at urinary alkalinization, was reported in seven accidents with a tricyclic antidepressant, most commonly amitriptyline, as the major causal agent. Alkalinization was the most commonly used method to enhance elimination, mainly because of its easy execution and wide availability. Annex 1 shows some substances that require urinary alkalinization.

Most patients who ingest a drug or are exposed to a toxic amount of substance can be managed with support measures and administration of a single dose of activated charcoal. Being at an ICU is a limiting factor related to the number of deaths, which shows the need for efficient support measures. Usually, 98% of the poisonings requiring ICU admission, adequate electrocardiographic monitoring, correction of fluid and electrolytic disorders, use of antidotes, use of MV, and other support measures recover. In our study, the need for MV did not seem to modify the outcome. However, the severity of ingestion or the

Annex 1 MAJOR METHODS TO ENHANCE URINARY ELIMINATION. INDICATIONS FOR URINARY ALKALINIZATION (UA), HEMODIALYSIS (HD), HEMOPERFUSION (HP), AND HEMOFILTRATION (HF)[8,11,13,14,22]

Toxic agent	UA	HD	HP	HF
Alcohols	–	YES	–	–
Acetone	–	YES	–	–
Acetaminophen[E]	–	YES	<u>YES</u>	–
2, 4 D- chlorophenoxyacetic acid (herbicide)	YES	–	–	–
Valproic acid	–	YES	YES	–
Aminoglycosides	–	YES	–	YES
Amitriptyline, Nortriptyline[**]	YES	–	–	–
Atenolol	–	YES	YES	–
Barbiturates	YES	YES	YES	–
Bromide	–	YES	–	–
Caffeine	–	–	YES	–
Carbamazepine	–	YES	<u>YES</u>	–
Chloramphenicol	–	–	YES	–
Chlorpropamide	YES	–	–	–
Dapsone	–	–	YES	–
Diflunisal	YES	–	–	–
Digitoxin 3	–	YES	–	–
Digoxin	–	–	YES	–
Disopyramide	–	–	YES	–
Ethanol	–	YES	–	–
Eticlorvinol[C, *]	–	–	YES	–
Ethylene glycol	–	YES	–	–
Phenylbutazone	–	–	YES	–
Phenytoin	–	–	YES	–
Phenobarbital[C]	YES	YES	YES	–
Fluorides	YES	YES	–	–
Gluthetimide[*]	–	–	YES	–
Isopropanol (isopropyl alcohol)	–	YES	–	–
Lithium	–	YES#	–	–
Meprobamate[*]	–	–	YES	–
Hard metals (possible)	–	YES	–	–
Methanol (and formic acid)	–	YES[#]	–	–
Methaqualone[*]	–	–	YES	–
Metformin[***]	–	YES	–	YES
Methotrexate	YES	–	YES	YES
Amanita fungi (amanitine and phalloidin)[A]	–	–	YES	–
Nadolol	–	YES	–	–
Paraquat[B # *]	–	–	YES	–
Primidone	YES	–	YES	–
Pentobarbital	YES	YES	<u>YES</u>	–
Procainamide	–	YES	YES	–
Salicylates	YES	YES[#]	<u>YES</u>	–
Sedatives-hypnotics	–	–	YES	–
Sotalol	–	YES	–	–
Sulfonamides	YES	–	–	–
Theophylline[#]	–	YES	<u>YES</u>	–
Carbon tetrachloride	–	–	YES	–
Thiocyanate	–	YES[##]	–	–
Trichloroethanol (Chloral hydrate)[D]	–	YES	YES	–

A: may be effective within the first 24 hours; B: high tissue binding reduces efficacy, unless installed at an early phase; C: indicated when support measures are not sufficient or when prolonged coma is expected; E: metabolite of chloral hydrate; F: indicated only for massive ingestions with very high serum levels (> 1,000 mg/L) complicated with coma and/or hypotension;

*: hemodialyzable, possible, but clearance equal to or lower than the usual body clearance makes its use impossible as a method to enhance depuration; **: may undergo hemoperfusion, possible, but clearance equal to or lower than the usual body clearance makes its use impossible as a method to enhance depuration; ***: dialyzable, with HD clearance lower than usual body clearance, but useful in management because of the correction of associated lactic acidosis, poisoning being more common in patients with kidney failure;

#: indicated immediately if poisoning is significant; ## : indicated in patients with kidney failure who develop high levels of thiocyanate during extended therapy with nitroprusside. Plays no role in cyanide poisoning;

Underlined: indicates the preferential method or superior reported clearance.

pharmacological properties of the poison requires the consideration of techniques to enhance its elimination in approximately 1% of the cases.[8] In this study, dialysis methods were the procedures used to enhance elimination and are described below.

The clinical efficacy of dialysis methods and HP in acute poisonings cannot be easily estimated, because the concomitant intestinal absorption, liver metabolism, and urinary excretion need to be considered.[11-14] Extracorporeal techniques can be useful in poisoning with salicylates, methanol, ethylene glycol, lithium, and overdoses of theophylline. However, they have limited use in poisonings with sedative-hypnotic substances and industrial and domisanitary products. When required, HD and HP should be available on an emergency basis.[7]

Hemodialysis is more useful in removing low molecular weight toxins, with a low volume distribution, a low degree of protein binding, high hydrosolubility, low endogenous clearance, and high dialysis clearance as compared with total body clearance.[11-14] In the case of poisoning with a drug whose HD clearance is significantly greater than endogenous clearance, the use of HD should be considered if the patient's condition deteriorates progressively or if the drug concentrations measured predict a worse prognosis when HD is not used. Usually, HD is indicated for a limited number of poisonings (Annex 1).

Clearance rates are greater with HP than with HD, if the adsorbent (activated charcoal or polystyrene resin) can bind to the toxin. The extraction rates for HP are close to 1.0 for some substances, and the clearance rates of the drugs are close to those of blood flow through the HP circuit.[11-14]

The usefulness of both methods is limited when most of the drug is found outside the extracellular fluid, because of the characteristics of liposolubility and/or high tissue bonding (similar to tricyclic antidepressants, digoxin, and calcium channel blockers). Similarly to the alcohol-dehydrogenase blockade induced by ethanol and fomepizole, HD is useful in accelerating the clearance of methanol and ethylene glycol, as well as that of their toxic metabolites, correcting metabolic acidosis and reducing sequelae in target organs and mortality associated with those poisonings.[15] Changes in the constitution of the dialysate, including an ethanol-enriched, bicarbonate-based solution, have been reported as a treatment for acute methanol intoxication.[15] Hemodialysis also increases substantially the elimination rate of isopropanol, salicylates, theophylline, and lithium, although data about clinical outcomes are scarse.[14,16]

Although the toxicity and pharmacokinetic properties of a drug determine whether those procedures are indicated in severe poisonings, in certain situations, toxicokinetics is different from pharmacokinetics at therapeutic levels. For example, in acute poisoning with valproic acid, that agent is usually considered non-removable with HD, because of its high protein binding (90%-95%). However, severe poisonings with very high doses of valproic acid can lead to saturation of the plasma protein binding, which results in an increase in the free fraction of the acid. That specific behavior makes HD or high-flow HD an effective treatment and HP relatively less effective, because of the rapid column saturation.[17-18]

Drugs adsorbed by activated charcoal can usually be extracted by use of HP. The removal rate exceeds that achieved by use of HD when the toxin has high protein binding, high molecular weight, or is liposoluble. With theophylline, for example, the extraction rate by use of HD is of approximately 50%, when compared with values of 99% at the beginning of HP (before saturation of the filter, which occurs in approximately two hours of therapy). However, the extraction rate only reflects the percentage of removal of the drug presented to the HD membrane or HP filter, because, for drugs with large tissue deposits, those techniques remove only a small fraction of the total body content, determining the need for one more session.[11-14]

The high extraction rates and clearance that can be obtained with those methods do not necessarily predict increased clinical efficacy or more favorable outcomes in poisoned patients. No controlled clinical study in poisoned patients has been performed to determine whether HP reduces morbidity or mortality, when compared with support measures. Evidence of clinical efficacy for HP is based on favorable pharmacokinetic data, studies with animals, anecdotic case reports, case series, and retrospective non-controlled studies comparing HP with support care for poisonings due to a diversity of drugs.[11-20] However, they do not allow a strong conclusion about the relative efficacy of several management strategies.

Hemoperfusion should be considered in severe poisonings, as those caused by bipyridyl compounds (paraquat and diquat). Although early use (beginning within the first 48 hours) is recommended, removal of large amounts of those compounds does not occur in a single session because of their characteristics of solubility and volume distribution.[8,14] Hemoperfusion is significantly more effective than HD to increase theophylline clearance, but it is associated with a higher rate of complications and is not available in all centers.

When available, HP is preferred over HD. Under certain circumstances, such as poisoning with acetylsalicylic acid, even when HD is performed, early urinary alkalinization is recommended to prevent acidosis and also to promote renal elimination.[21]

The choice of vascular access and anticoagulation for instituting HD or HP follows the usual indications and contraindications of the nephrological practice, whose discussion is out of the scope of this study. However, it is worth noting that the duration of dialysis in such cases does not consider the kinetics of urea and creatinine, but that of the toxic agent for which it was instituted. Intermittent therapy for poisoned patients usually lasts four to eight hours, but should be defined by the clinical response, the serum concentrations of drugs, and the method applied.[6-20] In certain poisonings and specific populations (such as carbamazepine in pediatric patients), high-flow HD can be as efficient as HP without the drawbacks of thrombocytopenia, coagulopathy, hypothermia, and hypocalcemia of the latter.[14] In the present study, only intermittent methods were used.

Our findings are in accordance with those available in the literature. Hemodialysis was performed only in 0.04% of all poisonings registered at AAPCC in 1996 and it slightly more than doubled in one decade (0.08% in 2008).[3,11] Our findings are similar (0.03%). The incidence of dialysis effectively performed was 11 out of 245 severe cases registered, the approximate annual incidence being 3.67 procedures/year (mean of one procedure for every 22.7 severe cases). On average, it is estimated that one dialysis was performed to every 3,278 human exposures to any toxic agent.

The fact that dialysis was indicated essentially according to traditional nephrological (and not toxicological) indications may have accounted for a considerable bias in the results. Thus it is of note the role of the nephrologist, as a consultant, considering the toxicological indication for dialysis in selected cases. The tendency towards associating dialysis with the risk of death, because of the increased incidence of death in those accidents, has not been confirmed. The small number of procedures performed has contributed to not achieving the required significance level. Hemodialysis and HP are not responsible for the undesired outcomes, although complications resulting from the institution of those procedures are inherent. The modality of treatment may have been applied late, aiming at preventing the clinical outcome of a situation, which, by itself, was foreseen as unfavorable (a bias in the option of conservative management *versus* early institution of a procedure).

That hypothesis leads to the following question: if instituted at an early phase, could dialysis reduce the death outcome? So far, that question is hard to answer, considering that most studies published involve case reports, case series, case-control studies or observation cohorts, in addition to the fact that the outline of a randomized clinical trial with human beings is difficult to implement from the bioethical point of view. However, at least one study compared the outcome in lithium poisonings managed with HD according to guidance from the local Poison Control Center with those not undergoing HD. In the specific case, the outcome of patients undergoing dialysis did not differ from that of those, who, despite the recommendation, did not undergo the procedure.[16]

It is worth noting that HF, although not used in the cases studied, has been used to eliminate aminoglycosides, vancomycin, and complexes of chelated metals, but the removal of drugs with high protein binding is not effective. It can be beneficial in poisonings with drugs with a high volume distribution, high tissue binding, or slow intercompartmental transference (such as procainamide). Successful continuous venovenous hemodiafiltration has been reported for lithium poisoning, without the drawback of hemodynamic instability and plasma level readjustment that can occur between dialyses in the intermittent process.[12]

Peritoneal dialysis is much less effective than HD or HP, being indicated only when those methods are not available, are contraindicated, or are not feasible (such as in neonates). It is always a method of exception and not of choice.[13]

Conclusion

Our incidence of performing dialysis is similar to that around the world. Despite the indication for a certain poisoning, the method was underused or had its institution delayed, which may have accounted for unfavorable outcomes. Thus, the method can be used in several types of poisonings. The small number of procedures obtained, although resulting from thousands of poisonings occurring over a period of three years in a population of approximately ten million inhabitants,[23] in addition to the fact that HD was indicated on toxicological bases, but effectively initiated according to nephrological bases, may have accounted for a bias in the results. The tendency to associate dialysis with a greater risk for death, not statistically confirmed, may have been due to the use of that therapy in more severe cases, and to the attempted use to minimize outcomes predicted as unfavorable. The issue is still controversial and should be further studied by use of alternative outlines.

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