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NEPHROTOXIC INJURY IN FATAL POISONINGS IN CHILDREN – ETIOLOGY AND PATHOLOGICAL ASPECTS

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Abstract

Introduction. The actual prevalence of toxic nephropathies in children is not fully known, because renal functional and structural changes caused by nephrotoxins are nonspecific.
The objective of the study was to evaluate the aetiology and renal involvement in severe poisoning with lethal potential in children.
Methods. We retrospectively analyzed a group of patients, aged between 0-18 years, with deaths due to acute intoxication, who were investigated at the National Institute of Legal Medicine „Dr. Mina Minovici" Bucharest, Romania, during a 9 years period. We analyzed the aetiology of deaths by poisoning in children, the aetiology and the frequency of nephrotoxic injury and the pathological aspects of nephrotoxic poisonings.
Results. From a total of 69 children deaths due to acute intoxication, the most common cause of death was acute poisoning with carbon monoxide (23 cases). The other etiologies were represented by multidrug poisoning – 9 cases, organophosphorus intoxications – 9 cases, and intoxications with illicit drugs – 8 cases. Acute renal injury was present in 20 patients, mainly in acute multidrug poisoning. The most common

Résumé

Etiologie et aspects pathologiques des lésions néphrotoxiques dans les intoxications mortelles chez les enfants

Introduction. La prévalence réelle des néphropathies toxiques chez les enfants n'est pas complètement connue car les modifications fonctionnelles et structurelles de la fonction rénale causées par les néphrotoxines ne sont pas spécifiques.
L'objectif de l'étude était d'évaluer l'étiologie et l'implication rénale dans les intoxications graves au potentiel létal.
Méthodes. Nous avons analysé rétrospectivement l'étiologie des décès par empoisonnement chez les enfants au cours d'une période de 9 ans, l'étiologie et la fréquence des lésions néphrotoxiques et les aspects pathologiques des empoisonnements néphrotoxiques.
Résultats. Sur un total de 69 décès d'enfants dus à une intoxication aiguë, la cause la plus fréquente de décès était une intoxication aiguë au monoxyde de carbone, soit 23 cas. Les autres étiologies: intoxication par plusieurs drogues – 9 cas , intoxications aux organophosphorés – 9 cas et intoxications par des drogues illicites – 8 cas . Des lésions rénales aiguës étaient

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aspect was tubular nephrosis in 15 cases, followed by the appearance of acute tubular necrosis in 10 cases, tubulo-interstitial nephritis in 1 case, and non-specific aspects with renal stasis in the remaining 6 cases.
Conclusions. Kidney involvement in pediatric poisoning is rare, but when acute kidney injury occurs, the prognosis of the intoxication becomes severe. Renal injury was present in 30% of cases, either by direct kidney damage with acute tubular necrosis, or by association of haemodynamic, cardiogenic, or septic shock.

Keywords: fatal poisoning, carbon monoxide, nephrotoxic, children poisoning.

présentes chez 20 patients, principalement dans les cas d'intoxication aiguë à plusieurs médicaments. L'aspect le plus courant était la néphrose tubulaire dans 15 cas, suivie de l'apparition d'une nécrose tubulaire aiguë dans 10 cas, d'un aspect de néphrite tubulo-interstitielle dans un cas et d'aspects non spécifiques avec une stase rénale dans les 6 autres cas.
Conclusions. L'atteinte rénale dans l'intoxication pédiatrique est rare, mais en cas d'atteinte rénale aiguë, le pronostic de l'intoxication devient grave. Des lésions rénales étaient présentes dans 30% des cas, soit par atteinte rénale directe avec nécrose tubulaire aiguë, soit par association de choc hémodynamique, cardiogénique ou septique.

Mots-clés: intoxication mortelle, monoxyde de carbone, néphrotoxique, empoisonnement des enfants

Introduction

The evaluation of severe acute poisoning with a lethal potential provides very useful data on the aetiology and the need of emergency treatment. The data obtained in this study bring information about the aetiology of deaths by poisoning in children, the aetiology, the frequency of nephrotoxic injury and the pathological aspects of nephrotoxic poisonings. The association of kidney injury in acute children poisoning requires rapid therapeutic decisions, to prevent its evolution and to improve the patient's prognosis[1-6].

The objective of the study was to evaluate the aetiology and the renal involvement in severe poisoning with lethal potential in children.

Material and methods

We retrospectively analyzed a group of patients, aged between 0-18 years old, with deaths due to acute intoxication, who were investigated at the National Institute of Legal Medicine „Dr. Mina Minovici". Bucharest, Romania, during a 9 years period. We analyzed the aetiology of deaths by poisoning in children, the aetiology and the frequency of nephrotoxic injury and the pathological aspects of nephrotoxic poisonings. We obtained the data from the registry, death certificates and medical records.

Results and discussion

During the analyzed period in the Institute „Dr. Mina Minovici", 69 deaths by acute intoxication were recorded in the 0-18 years age group. We analyzed the aetiology of deaths by poisoning in children, the aetiology and frequency of nephrotoxic injury and the pathological aspects of nephrotoxic poisonings.

Epidemiological data

The age distribution was: 0-1 year: 6 cases (13%), 1-5 years: 22 cases (32%), 6-12 years: 11 cases (16%) and 12-18 years: 30 cases (43%) (Figure 1).

The average age was 9 years. Two peaks were observed: 1-5 years old, the age group where accidental intoxication is the most common, and the 12-18 years old age group, that includes volitional suicidal and parasuicidal poisoning. In our analysis, we emphasize the existence of a significant number of intoxications in the 0-1 year age group; although acute intoxications are not common, their death potential may be very severe. Gender distribution was as follows: 35 cases of death through acute poisoning in girls (51%) and 34 cases of acute poisoning deaths in boys (49%); the distribution does not have significant statistical significance.

The distribution of deaths by the environment is balanced; there is a mild predominance of cases from the urban environment (36), compared to those from the rural environment (33).

Etiology

From a total of 69 children deaths due to acute intoxication, the most common cause of death was acute poisoning with carbon monoxide, which accounted for 23 cases, representing 33% of the total. The other etiologies were represented by multidrug poisoning – 9 cases (13%), organophosphorus intoxications – 9 cases (13%) and intoxications with illicit drugs – 8 cases (12%). There were also recorded cases of caustic poisoning – 5 cases (7%), poisoning with

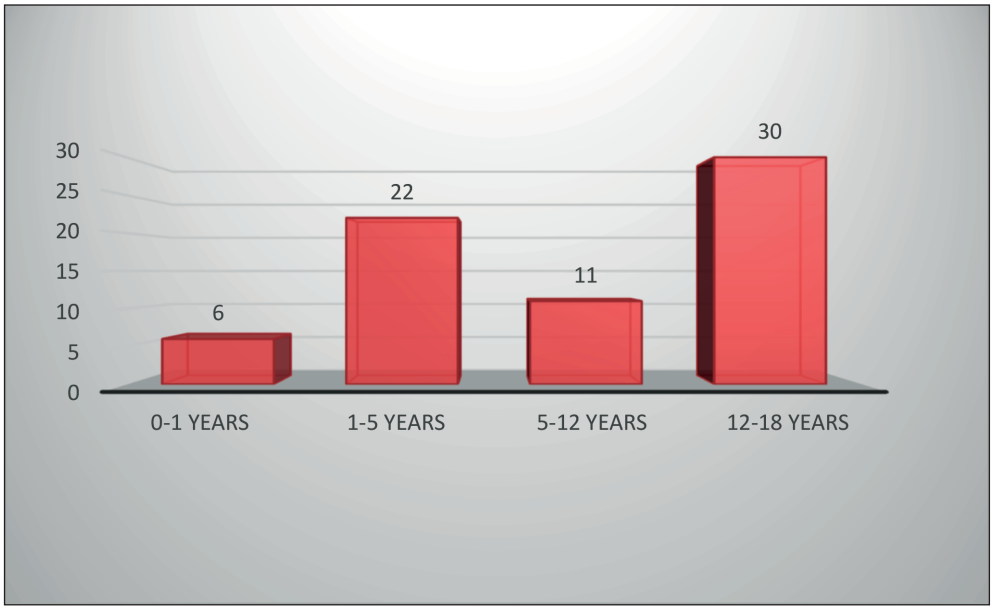

Figure 1. Age distribution of patients with deaths by acute intoxication.

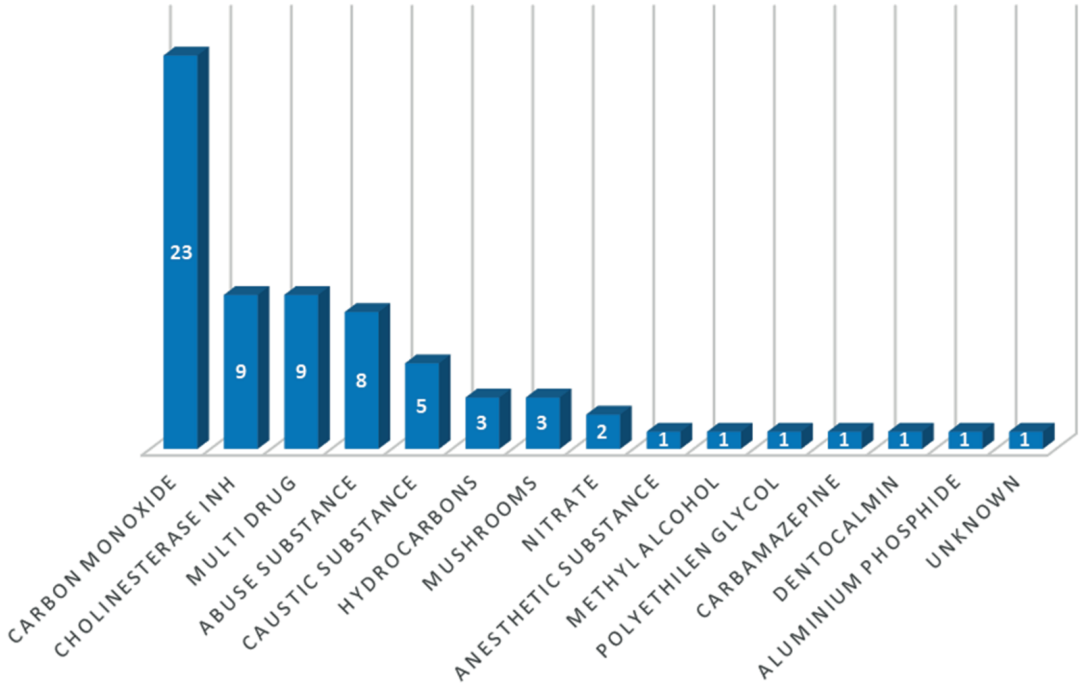

Figure 2. Etiology of poisonings in children.

hydrocarbons – 3 cases (4%), mushrooms – 3 cases (4%), nitrite – 2 cases (3%), 1 intoxication case with polyethylene glycol, methyl alcohol, dentocalmin, aluminum phosphate, carbamazepine and anesthetics[7-11].

There is a clear predominance of deaths through acute poisoning with carbon monoxide, a significant cause of home death, mostly accidental, reported as most prevalent also in studies conducted in other countries[12-16]. Among the multidrug poisonings, we observed that most of them occurred in the age group of 12-18 years, with serious drug intoxication, the most commonly involved substances being anti-inflammatory and analgesic drugs, oral antidiabetics, tricyclic antidepressants, benzodiazepines and barbiturates.

Of these, we highlight a serious acute intoxication with colchicine and metamizole, and one with

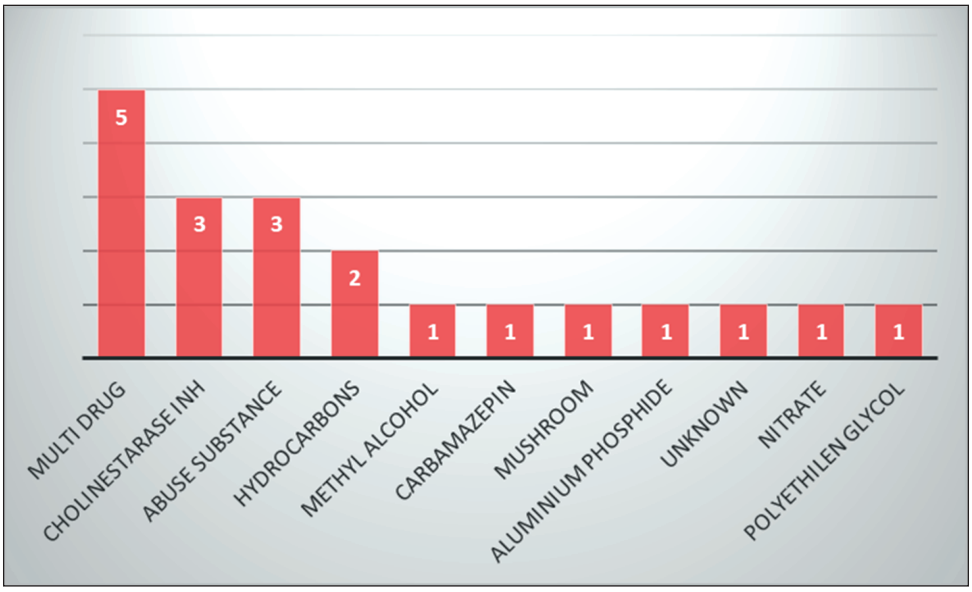

Figure 3. Etiology of nephrotoxic poisonings in children.

metformin and metamizole, that evolved with severe acute renal insufficiency. Acute intoxications with cholinesterase inhibitors had two major etiologies, Furadan and Diazinon, and were mostly accidental intoxications. In drug poisonings, heroin was most commonly involved, followed by methadone, morphine and codeine. In the case of poisoning with caustic substances, sodium hydroxide was the main cause of death, and in the case of hydrocarbon poisoning diesel was the main cause. The nitrate poisonings caused death in two infants who were fed with milk that was prepared with fountain water[17-20] (Figure 2).

With regard to the correlation between the living area and the etiology, we observed that, in both urban and rural areas, carbon monoxide poisoning is the main cause of death, but we also noted some significant differences between the two areas, namely an increased frequency of deaths through acute poisoning with organophosphorus, caustic substances and hydrocarbons in the rural area compared to the increased frequency of deaths due to acute multidrug poisoning and with illicit drugs in the urban areas. Regarding the place where death occurred, 43 deaths occurred in a hospital environment, compared to 26 home deaths that came directly to the Institute „Dr. Mina Minovici". Of these 26 cases, most were carbon monoxide intoxications[21-22].

Histopathology analysis

We further analyzed the presence of acute renal injury immediately or in the evolution of patients who died of acute intoxication. Of the 69 cases, acute renal injury was present in 20 patients, representing 29% of the total deaths.

It is noticed that acute renal injury was present mainly in acute multidrug poisoning. The 5 cases were 4 voluntary intoxications involving associations of nonsteroidal antiinflammatory drugs (NSAIDs), analgesics in 2 cases, colchicine and metamizole in one case, and oral antidiabetic and metamizol in the other case, and 1 accidental home intoxication with aminophenazone, caffeine and nifedipine (Figure 3).

Of the 69 deaths analysed in 33 cases, no histopathological examination was performed. From the 36 histopathologically evaluated cases, in 32 of them the kidney tissue was analysed. The most common aspect was tubular nephrosis in 15 cases, followed by the appearance of acute tubular necrosis in 10 cases, tubulo-interstitial nephritis in 1 case, and non-specific aspects with renal stasis in the remaining 6 cases. Of the 10 cases with acute tubular necrosis, 6 of them also had an important hepatocyte necrosis, compared to only 4 cases in the tubular nephrosis group. It should be noted that 9 of the patients with acute tubular necrosis showed clinical or paraclinical signs of acute renal injury, the 10th died at home after carbon monoxide poisoning. In the 12 patients with tubular nephrosis, signs of acute renal injury were present in 2 cases. Acute kidney injury has also been associated with tubulo-interstitial-nephritis. The appearance of tubular nephrosis was associated especially with cases that have evolved with toxic or septic shock, such as severe poisonings with hydrocarbons and caustic substances, or in poisonings that evolved with cardiogenic or hemodynamic shock, such as with dentocalmin and carbamazepine poisonings [23] (Figure 4).

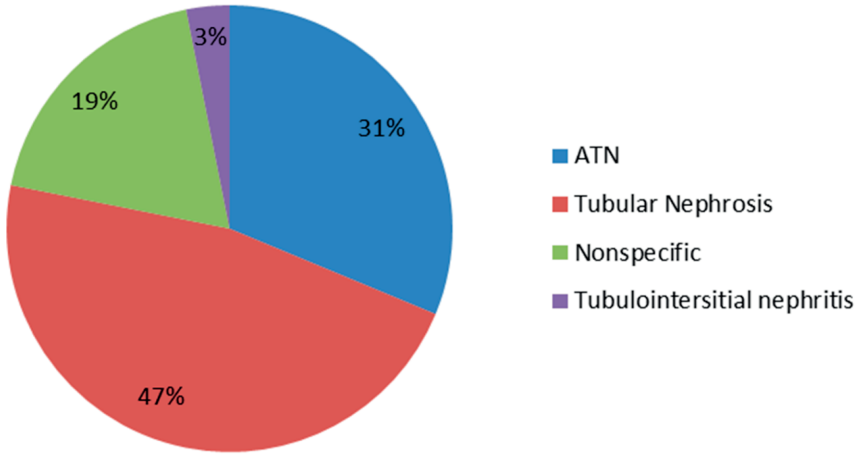

Figure 4. Histopathology aspects of nephrotoxic poisonings.

Conclusions

Deaths from acute poisoning in children are rare. In our study, carbon monoxide poisoning was the main etiology, representing 33% of all deaths by poisoning. Regardless of the environment of origin, these are preventable poisonings; there is a need for a better education of the population and use of methods of prevention. Kidney involvement in pediatric poisoning is rare, but when acute kidney injury occurs, the prognosis of the intoxication becomes severe. Renal injury was present in 30% of cases, either by direct kidney damage with acute tubular necrosis or by association of haemodynamic, cardiogenic, or septic shock. Judicious use of nephrotoxic drugs with proper hydration is the most important measure for the prevention of toxic renal injury during hospitalization. Prevention of renal toxicity has to be based on very good knowledge of the toxins frequently involved in severe poisonings, that cause liver and kidney failure, acute circulatory insufficiency or direct kidney toxicity. The treatment of these types of intoxications should also include methods of enhanced elimination, that can greatly reduce the risk of death by serious toxic nephropathy[24-25].

Compliance with Ethics Requirements:

„The authors declare no conflict of interest regarding this article"

„The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. The study was approved by the ethics committee"

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