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Interest of toxicological analysis in patients admitted to a pediatric emergency department

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Abstract

Objective: Evaluate the interest of toxicology screening in the management of patients in a pediatric emergency department, by assessing its diagnostic utility.

Patients and Methods: This is a retrospective cross-sectional study conducted over two years in the Emergency Department of the Abderrahim Harouchi Mother and Child Hospital, of the Ibn Rochd University Hospital in Casablanca, Morocco. We included all children who underwent qualitative toxicological screening by Gas Chromatography coupled with Mass Spectrometry (GC/MS). A descriptive analysis was conducted on the clinical and toxicological characteristics of the patients. The contingency test allowed us to compare the context of the toxicological screening request and its diagnostic utility.

Results: Eighty-seven children were included, with a Male-to Female sex ratio of 1.2. The age of the patients ranged from 1 month to 14 years, with a median of three years. Among the included population, 119 screenings were performed. Drugs were implicated in 27 cases, while 4 pesticide intoxications were found, including carbofuron, chloralose, methomyl and terbucarb, along with 2 cannabis intoxications. A proportion of 88% of screening requests, made in the absence of clinical guidance, turned out to be positive, accounting for 31% (24 cases out of 77) ($p<0.001$).

Conclusion: Toxicological analysis is a valuable tool to assist the clinician in managing intoxications by confirming or excluding the toxic hypothesis. However, toxicological analysis can only be useful and effective, avoiding analytical pitfalls, in the presence of dialogue between the clinician and the analyst.

Keywords: Intoxication; Screening; Emergencies; Toxicological Analysis; Children

1. Introduction

Poisoning are a frequent reason for consultation in pediatrics. They represent one of the principal causes of morbidity and mortality in the world and constitute a significant public health issue [1]. The total number of poisoning pediatric recorded in Poison Control Centre and emergency pediatric department is increasing steadily [1–4]. These intoxications accounted for 50% of the reported intoxication notifications to American poison control in 2017 [5]. Approximately

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30% of all reported cases in 2021 at the Moroccan Poison control Center (MPCC) concerned the age group of baby walker (one to five old years) [6]. This age group is also the most affected by accidental poisoning in Tunisia [7].

Diagnosing an intoxication in children is not always easy and obtaining a medical history can sometimes be impossible. Additionally, parents may deny the presence of an intoxication out of fear of being accused of abuse or neglect. Therefore, performing toxicological analysis is crucial as it allows us to rule out an intoxication, identify a toxic etiology not suspected at the time of hospitalization, confirm the suspected toxic agent (e.g. ingestion of cannabis resin or ethanol), or exclude or reveal an association with other xenobiotics (e.g. inappropriate administration of an analgesic) [8,9].

Moroccan literature is limited to studies conducted by the MPCC laboratory, which showed that 36.1% of analysis requests in 2017 were related to pediatric intoxications [10] and 58.8% in 2018 [11]. In this context, the objective of our study was to highlight the importance of performing toxicological analysis in a pediatric emergency department by evaluating their usefulness in confirming or denying toxic etiology.

2. Material and methods

We conducted a descriptive retrospective cross-sectional study over a period of 2 years, from January 1st, 2021 to January 10th, 2023, at the Pediatric Emergency department of the Abderrahim Harouchi Mother and Child Hospital at the Ibn Rochd University Hospital Center in Casablanca.

We included all children aged one month to 14 years old and hospitalized in the Short-Term Hospitalization Unit of the service for an intoxication with unknown products or having an unexplained sudden onset symptomatology. Children intoxicated from volatile industrial products, insect stings or bites, or bites from venomous animals were excluded from this study.

The data were collected from the patient's medical record using a pre-established exploitation sheet. We included the patient's age, sex, date of arrival at the emergency department, as well as clinical characteristics. The samples collected included whole blood collected in in EDTA tubes, urine in dry tubes without preservatives, and gastric lavage fluid, then stored in the refrigerator (between +2 °C and +6 °C) until transport to MPCC-LAB. Toxicological screening or broad toxic substances in the various matrices, also known as screening toxological, was conducted in two steps:

The first step involves an emergency toxicological screening using a urine cassette test via an immunochromatographic techniques (NarcoCheck®) of the "No/Yes" type, which provides either a "negative" or "positive" result for each drugs or medicines. The detection threshold indicated for this type of test were 300 ng/ml for benzodiazepines, barbiturates and morphine, 1000 ng/ml for tricyclic antidepressants, and 50 ng/ml for tetrahydrocannabinol (THC), a metabolite of cannabis (marijuana, hashish).

The second step is a confirmation and qualitative toxicological screening search in urine, blood, gastric lavage fluid, and samples of implicated products in cases of intoxication brought by the victim's entourage. This screening was conducted using gas chromatography coupled with mass spectrometry (Clarus® 680 GC- PerkinElmer, Clarus® SQ 8C).

The capillary column used is an Rxi®-5ms 5% diphenyl/95% dimethyl polysiloxane column (30 m x 0.25 mm ID, 0.25 µm film thickness). The injector temperature is set to 280 °C and operated in splitless mode. Helium is used as the carrier gas with a fixed flow rate of 1mL-min-1, the column temperature is set at 40 °C, maintained for one minute after injection. The final temperature of 300 °C is reached at a rate of 15 °C-min-1 and held for 5 minutes. Electron impact detection is conducted at 70 eV in scan mode. Data processing is performed using TurboMass version 6.0 software, and the spectral library used is NIST version 2014. The sample undergoes liquid-liquid extraction. Prazepam is used as an internal standard. The extraction solvent is a mixture of dichloromethane, 2-propanol and heptane (25, 10, 65, v/v/v). The extract is evaporated under nitrogen at 40 °C. The dried residue is reconstituted in 100 µL of methanol, of which 50 µL was is transferred to a vial for GC-MS analysis.

Data analysis was conducted using SPSS version 23 software. Descriptive analysis focused on patient characteristics (age, sex ratio), reasons for hospitalization, and the results of various toxicological analyses.

Values of $p<0.05$ were considered statistically significant. The contingency test (chi-square or Fisher's exact test) was used to compare the context between the context of toxicological screening request (absence of clinical orientation of the diagnosis, intoxication with unknown products) and its diagnostic utility.

3. Results

Eighty-seven children were included. The age ranged from one month to 14 years, with a median of 3 years. The sex ratio (M/F) in the study was 1.2, with 38 (43.6%) females and 49 (53.3%) males.

Toxicological analysis requests were made in a context of absence of clinical orientation, presenting unexplained sudden clinical signs in 77 (88%) of cases, while 10 (12%) of patients were admitted in a context of intoxication but the toxic or product was not identified.

During this two-year study, 87 children included underwent a screening, which corresponds to 0.14 request per 100 patients of all admissions during the same period. A total of 119 analyses conducted on 77 (64.7%) blood samples, 39 (32.7%) urine samples, one gastric lavage fluid (Figure 1), and two suspected product samples, one being a blue liquid and the other a violet powder (Figure 2). The rapid urinary analysis for toxic substances detection was positive in 17(43.5%) out of 39 urine samples, with a predominance of the benzodiazepine class in 10 (58.8%) cases, followed by four (28.5%) positive cases for barbiturates, two (11,7%) cases positive for tetrahydrocannabinol (THC) and one (5.8%) case positive for cotinine (Figure 3).

Out of 119 broad toxicological screenings conducted by GC-MS in various biological matrices and out of the two product samples, 49 (41.1%) samples tested positive with the identification of at least one molecule (Figure 4). The positive samples for toxic drugs detection were as follows: 28 (57.1%) blood samples, 19 (38.7%) urine samples, and two (4%) product sample specimens (carbofuron for the violet powder and methomyl for the blue liquid). The analytical yield was thus 41.1% (49/119). The toxicological screening enabled us to (Table 1); confirming a suspected intoxication in nine (90%) out of ten cases and, identifying an etiology in the absence of clinical guidance in 24 (31.2%) out of 77 cases.

Table I Diagnostic utility depending on the context of toxicological screening request

Context of prescription / Diagnostic utility	**Lack of direction N=77**	**Evident toxic etiology N=10**	**P-value**
Positive (confirmation or discovery of a toxic etiology)	24 (31,2%)	9 (90%)	0.001
Negative (exclusion of a toxic etiology)	53 (68,8%)	1 (10%)	

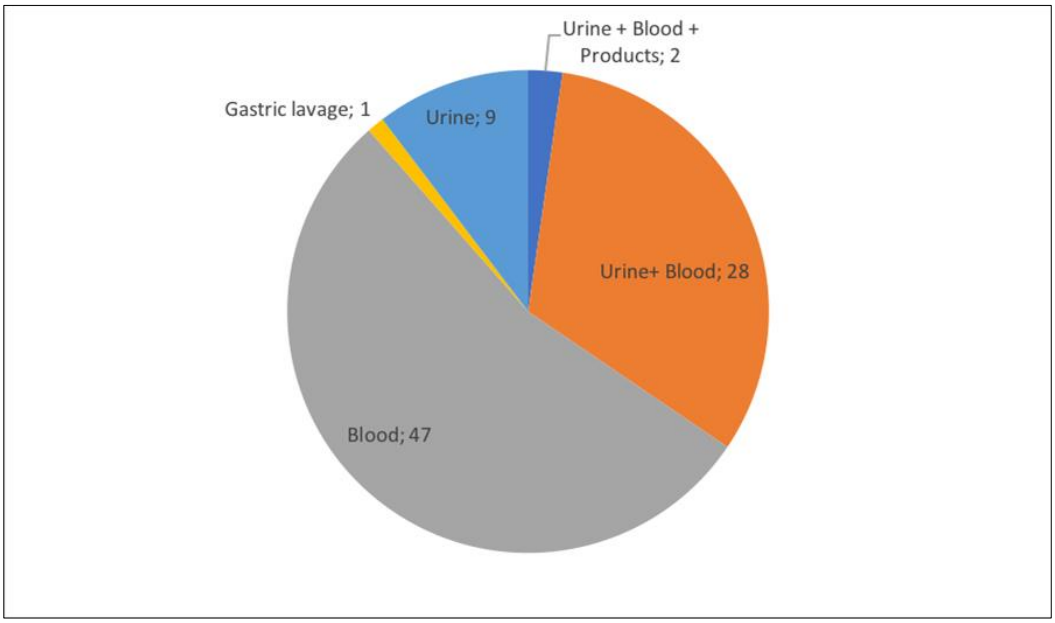

Figure 1 Distribution of patients according to by types of sampling (n=87)

4. Discussion

The median age in our series was 3 years, consistent with studies indicating that children under five years of age represent the largest percentage of intoxicated cases worldwide [1,5].

The sex ratio (M/F) in our study was 1.2, in line with a French study [12]. This observation is also supported by the literature, which suggests that among young children, male are more commonly exposed to accidental poisoning, while during puberty, girls exhibit a higher of intentional poisoning [13,14].

Toxicological screening was requested in 87 (14%) patients in our study, in contrast to 49 (75%) in a Tunisian study [7]. This percentage remains low, and does not truly reflect the magnitude of acute poisoning observed in pediatrics. The limited requests could be attributed to the unavailability of a toxicology laboratory at the University Hospital Centre where our study was conducted. In our series, 77 (88%) requests were made without clinical referral to the MPCC laboratory, compared to 42-51% in the literature [15,16]. However, requests for toxicological analysis in cases of intoxication by an unknown product accounted for 10 (12%) cases in our study, compared to 56 (25%) in the literature [15].

In the year 2013, a multidisciplinary working group on "Toxicology and clinical biology" from the SFTA- SFBC-STC-SRLF-SFMU-CNBH recommended that broad toxicological screening should only be used in the following situations: "If the clinical course and/or additional investigations are inconsistent with the initial toxidrome and patient history" and "In cases of circulatory failure or unexplained coma"[17].

These conditions were present in 77 (88.5%) out of 87 of our patients. Nonetheless, it would be valuable to formulate recommendations tailored to our context, drawing upon the expertise of pediatric, resuscitator pediatrics, and toxicology disease specialists.

The compounds in question are primarily drugs that primarily affect the nervous system, as shown by several studies [10,14,17–18]. A positive test result is not conclusive for diagnosis an intoxication. It may merely indicate therapeutic impregnation (in hospital or outpatient). Only the quantification of a specific molecule can make the difference.

Similar results have been documented regarding pesticide poisoning (carbofuron, chloralose, methomyl, terbucarb), with prevalence of 3%, 7% and 20% respectively in Qatar, India and Tunisia [7,14,21]. In Morocco, between 2008 and 2016, 25.7% of reported pesticide poisoning from Poison Control Centre of Morocco involved by pediatric population [22].

We identified 2 (11.7%) cases of cannabis intoxication, consistent with findings from other studies [4,9,23].

Toxicological screening yielded negative results in 54 (78.8%) cases in our study, while M-A. Champigny et al. reported 52% negative screening in a similar population [19]. This variance may be attributed to several factors, including differences in analysis techniques, the delay between intoxication and sample collection or the higher detection threshold compared to circulating levels.

Gas chromatography coupled with mass spectrometry retains its limitations in toxicological screening. This technique is primarily suited for volatile compounds or those likely to be vaporized and thermostable. Interpretation of the results must also consider toxicokinetics, toxic effects based on age [8,24,25], the time between admission and the sample collection, which may explain the decrease in detectable concentrations of certain xenobiotics [17].

The ideal approach to toxicological screening is to combine multiple techniques [24] and to search for xenobiotic metabolites [26]. This will help reduce the risk of false negative results. In our case series, toxicological screening confirmed intoxication in 9 (90%) out of 10 children. In these cases, the clinical presentation or toxic syndrome directed the pediatrician towards a family of toxic, even though this type of toxicant was unknown during questioning. This observation varied according to studies and years (22% to 53%) [7,18].

Limitations

This was the first study in Morocco and in public hospitals. But this study is not included all the services or all the hospitals. The results of this study, based on a small sample size, will be used to design an intervention study focusing on several different strategies. However, this study suffers several limitations including missing data and the unavailability of some medical records.

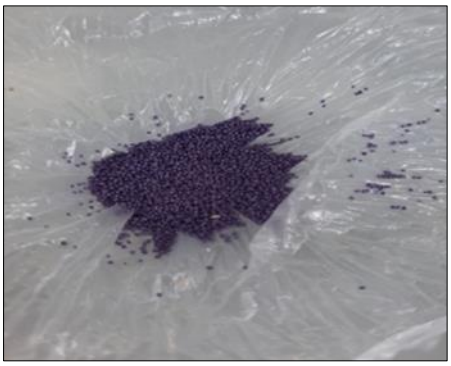

Figure 2 A sample of a suspected product

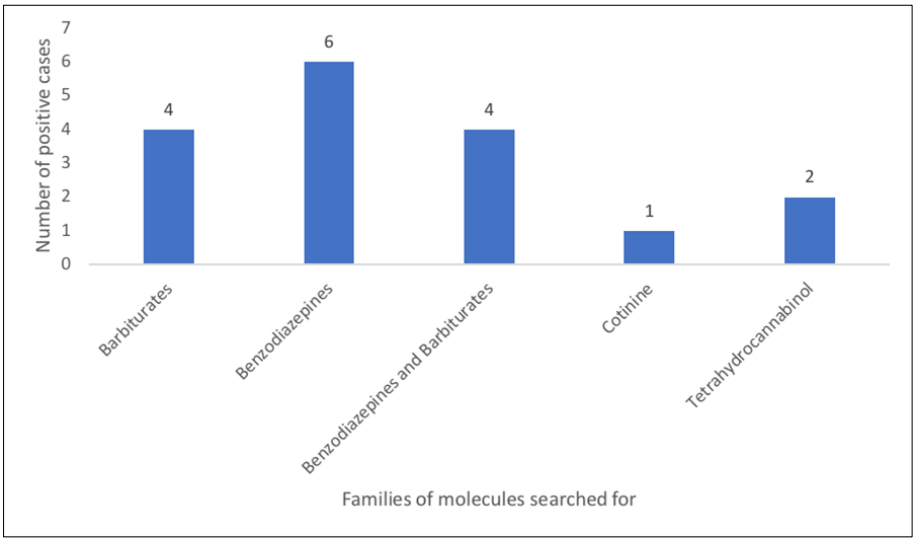

Figure 3 Results of rapid urine immunoassay analysis

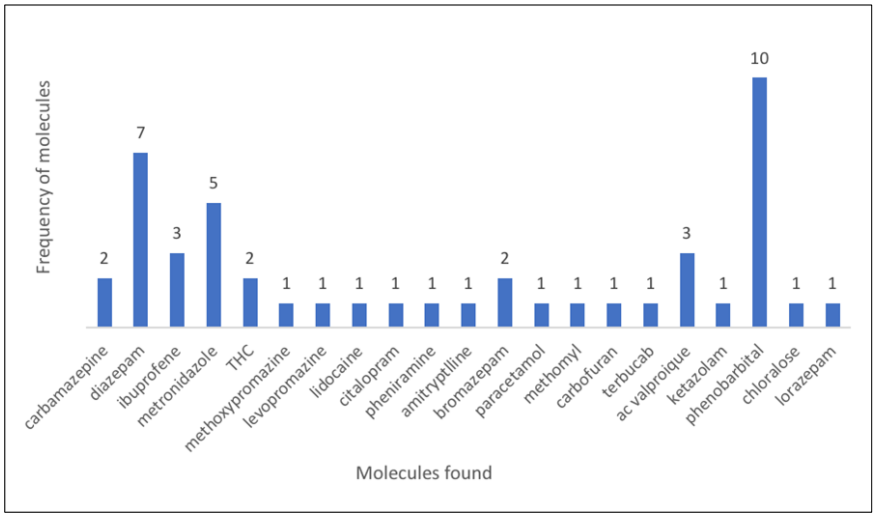

Figure 4 Frequency of different molecules found at (GC-MS) in the blood, urines, gastric liquid and of a suspected product

This study is a retrospective review of hospital records, and therefore subject to several additional limitations that should be noted explicitly. For example, some cases may have been missed or misclassified by clinicians. The separative analytical methods employed in this study could not be exhaustive, as only GC-MS was utilized. Although it serves as a reference method for numerous molecules, it remains inadequate for detecting all the molecules present in the sample.

The absence of poison control teams in the hospital has made transportation under suitable conditions and within a timely manner challenging, potentially resulting in the degradation or alteration of the collected samples.

5. Conclusions

Toxicological analysis is valuable in the management of poisoning in pediatrics, helping to avoid excessive additional investigations. Dialogue between the clinician and the analyst is crucial for better orientation and selection of methods to use.

Toxicological analysis is particularly benificial in this type of population as it allows for the identification of toxic agents and a anticipates patient management, especially in cases where medical history is difficult or incomplete

Compliance with ethical standards

Acknowledgment

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Disclosure of conflict of interest

Authors declare that there is no conflict of interests.

Statement of ethical approval

'The present research work does not contain any studies performed on animals/humans subjects by any of the authors'.

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