U.PORTO

MESTRADO

MEDICINA LEGAL

Paediatric Poisoning in children and adolescents admitted to the Emergency Unit of the Hospital de São João (Porto, Portugal), 2010-2018

Diana Paiva Ferreira

D

2022

U.PORTO

Diana Paiva Ferreira. Paediatric Poisoning in children and adolescents admitted to the Emergency Unit of the Hospital de São João (Porto, Portugal), 2010-2018

D.ICBAS 2022

Paediatric Poisoning in children and adolescents admitted to the Emergency Unit of the Hospital de São João (Porto, Portugal), 2010-2018

Diana Paiva Ferreira

INSTITUTO DE CIÊNCIAS BIOMÉDICAS ABEL SALAZAR

Diana Paiva Ferreira

Paediatric Poisoning in children and adolescents admitted to the Emergency Unit of the Hospital de São João (Porto, Portugal), 2010-2018

Tese de Candidatura ao Grau de Mestre em Medicina Legal, submetida ao Instituto de Ciências Biomédicas Abel Salazar (ICBAS) da Universidade do Porto

Orientadora: Doutora Diana Cristina Dias da Silva

Categoria: Professora Auxiliar Convidada & Investigadora

Afiliação: Instituto Universitário de Ciências da Saúde (IUCS) & UCIBIO/REQUIMTE, Laboratório de Toxicologia, Faculdade de Farmácia da Universidade do Porto, Porto, Portugal

Coorientadora: Doutora Maria José Pinto da Costa

Categoria: Professora Associada

Afiliação: Instituto de Ciências Biomédicas Abel Salazar (ICBAS) da Universidade do Porto, Porto, Portugal

Coorientador: Doutor Ricardo Jorge Dinis de Oliveira

Categoria: Professor Catedrático

Afiliação: Instituto Universitário de Ciências da Saúde (IUCS), Gandra, Portugal

Acknowledgments

À Professora Doutora Diana Dias da Silva, minha Orientadora, pelo seu acompanhamento, profissionalismo e pela partilha do seu conhecimento.

À Professora Doutora Maria José Pinto da Costa, minha Coorientadora, e ao Professor Doutor Ricardo Jorge Dinis de Oliveira, meu Coorientador, pela sua disponibilidade e presença.

Agradeço aos meus pais, ao meu padrinho, à minha avó, aos meus amigos e ao Lucas por acreditarem em mim, apoiarem-me durante todo este processo e não me deixarem desistir dos meus sonhos. Todos eles representam aquilo que sou hoje e, de alguma forma, incutiram os valores *major* na minha vida: honestidade, empenho, humildade e respeito.

Agradeço também a toda a equipa da Farmácia de Santa Clara por toda a disponibilidade e amizade.

Muito obrigada a todos!

Resumo

As intoxicações agudas, são a terceira causa de morte acidental na população infanto-juvenil europeia, e permanecem uma causa evitável de morbidade e mortalidade, mundialmente. O conhecimento sobre o padrão e a dimensão das intoxicações pediátricas em regiões específicas são imperativos para o desenvolvimento e promoção de estratégias e medidas preventivas para esses locais. Em Portugal, a epidemiologia das intoxicações em crianças com idade até aos 18 anos ainda não foi devidamente estudada, requerendo informações exaustivas sobre a prevalência e as características das intoxicações. Assim, o objetivo deste trabalho foi examinar retrospetivamente os casos de intoxicação na população apresentada ao Serviço de Urgência Pediátrica de um hospital terciário, localizado no Norte de Portugal.

Este estudo visou pacientes com idade inferior a 18 anos admitidos na Unidade de Emergência Pediátrica do Centro Hospitalar de São João (CHSJ), EPE, Porto (Portugal), entre 2010 e 2018. Os dados relacionados com a intoxicação (como o tipo de intoxicação, a intenção, o agente tóxico responsável, o tratamento, a evolução e o resultado clínico) e as características das crianças (idade, género, ciclo escolar, a origem, etc.) foram obtidos dos relatórios médicos e da base de dados do hospital.

Ao longo dos 8 anos de estudo, as intoxicações pediátricas corresponderam a 1.584 admissões hospitalares. A maioria dos casos eram referentes a adolescentes que se apresentaram por conta-própria devido à ingestão de um ou mais agentes tóxicos (principalmente álcool, medicamentos e drogas ilícitas). Uma segunda tendência foi observada em crianças mais pequenas (maioritariamente do sexo masculino), que foram trazidos para a urgência acidentalmente intoxicados por medicamentos e produtos domésticos. Em relação aos medicamentos, os que atuam no sistema nervoso central foram o tóxico mais prevalente. Não foram reportados óbitos e apenas 2,8% dos pacientes foram internados. As intoxicações ocorreram sobretudo ao fim de semana e durante o inverno e primavera.

De acordo com os nossos resultados, devem ser adotadas medidas para limitar a utilização de álcool e drogas ilegais nos adolescentes. Também é importante o desenvolvimento de programas para aumentar a literacia relativamente aos medicamentos e produtos domésticos (e.g., armazenamento) para prevenir a intoxicação de crianças muito pequenas. O nosso estudo incidiu apenas numa região de Portugal, pelo que devem realizar-se outros estudos a nível nacional, permitindo comparação de resultados e medidas preventivas de causas especificas para outras regiões.

***Palavras-chave**:* Envenenamento; Intoxicação; Pediatria; Epidemiologia; Medicamentos.

Abstract

Acute poisoning is the third leading cause of accidental death in the European child and youth population and remains a preventable cause of morbidity and mortality worldwide. Knowledge on the pattern and scale of paediatric intoxications in specific regions is imperative for the development and promotion of specific preventive strategies and measures for such locations. In Portugal, the epidemiology of poisoning in children ≤ 18 years has not yet been properly studied, requiring comprehensive information on the prevalence and intoxication characteristics. Thus, the objective of this work was to retrospectively examine the intoxications in the population presented to the Paediatric Emergency Department of a tertiary hospital located in the North of Portugal.

This study included the patients under the age of 18 admitted to the Paediatric Emergency Unit of Centro Hospitalar de São João, EPE (CHSJ), Porto (Portugal), between 2010 and 2018. Data related to intoxication (such as the type of intoxication, intent, toxic agent involved, treatment, course, and clinical outcome) and children's characteristics (age, gender, school cycle, origin, etc) were obtained from medical reports and hospital database.

Over the 8 years of the study, paediatric intoxications corresponded to 1584 hospital admissions. Most of the cases related to teenagers who presented themselves to the emergency room due to intentional ingestion of one or more toxic agents (mainly alcohol, pharmaceuticals, and abuse drugs). A second trend was observed concerning younger children (mainly males) who were brought to the urgency accidentally intoxicated by pharmaceuticals and household products. In what concerns pharmaceuticals, those acting on the central nervous system were the toxic most prevalent. No deaths were reported and only 2,8% of the admitted patients were hospitalized. Poisonings occurred mostly at weekends and during winter and spring.

In view of our results, measures should be adopted to limit the use of alcohol and illegal drugs. It is also important to develop programs to increase literacy regarding medicines and household products (e.g., storage) to prevent intoxication in toddlers. Our study only focused one region of Portugal, so further research should be carried out to at the national level, allowing comparison of results and tailored cause-specific preventive measures for other regions.

Keywords: Poisoning; Intoxication; Paediatrics; Epidemiology; Pharmaceuticals.

Index

Index of Figures

Index of Tables

Abbreviation list

5-HT- Serotonin

AAPCC- American Association of Poison Control Center's

AChE- Acetylcholinesterase

ADH- Alcohol Dehydrogenase

BAC- Blood Alcohol Concentration

BZD- Benzodiazepine

CBD- Cannabidiol

CHSJ- Centro Hospitalar de São João, EPE

CIAV- Centro de Informação Antivenenos

CNS- Central Nervous System

CO- Carbon Monoxide

GABA- Gamma-Aminobutyric Acid

GI- Gastrointestinal

HCN- Hydrogen Cyanide

ICD-9- International Classification of Diseases, Ninth Revision

LSD- Lysergic Acid Diethylamide

MDMA- 3,4-Methylenedioxymethamphetamine

NPS- Novel Psychoactive Substance

NSAID- Non-Steroidal Anti-inflammatory Drug

OTC- Over the Counter

OUD- Opioid Use Disorder

PCP- Phencyclidine

TCA- Tricyclic Antidepressant

THC- Delta-9-tetrahydrocannabinol

USA- United States of America

WHO- World Health Organization

1. Introduction

Acute intoxication in children is one of the most frequent causes for admittion to the emergency room, and one of the main public health problems. (Alinejad et al., 2017; Sawicka et al., 2019; Zhang et al., 2018). Annually it accounts for more than one million morbidities worldwide (Alinejad et al., 2017; Sawicka et al., 2019; Zhang et al., 2018). Acute intoxication is defined as the exposure to an exogenous chemical in a period less than 24 hours that can cause clinical manifestations and/or death (Abbas et al., 2012; Calabuig, 2004; F. F. Oliveira & Suchara, 2014; Zhang et al., 2018). According to 1998 American Toxic Exposure Surveillance System, 2.2 million cases of poisoning were reported annually in the United States (US), with 1.5 million of these cases corresponding to children and adolescents (Pawłowicz et al., 2013). The characteristics of the intoxications including the toxic agents, risk factors and epidemiology, show variability in distinct countries and even in different regions of the same country (Ahmed et al., 2015; Malangu, 2008; Pac-Kozuchowska et al., 2016; Pawłowicz et al., 2013; Sawicka et al., 2019). This variation occurs because children are affected by social, occupational, economic, and cultural prevailing practices, as well as the disposal of toxics (Azab et al., 2016). Therefore, when evaluating intoxicated children, it is useful to have information about common intoxication agents, aspects of the patient (additional intoxications, nutritional status, family socioeconomic status, family size, among others) and the progress and effects of the toxicant in the body (type, blood concentration, dose and means of exposure to the substance, symptoms) (Gokalp, 2019; Lee et al., 2019). In addition, the time elapsed from the transport of patients and the interventions made at the health facility is crucial for the prognosis. The duration often varies on the location of the medical service and transport conditions in the region (Gokalp, 2019).

Many studies published in the recent years detailed the patterns of paediatric intoxications worldwide. For instance, Domingos et al (2016) reported a total of 694 cases of children ≤14 years of age diagnosed with poisoning in Brazil between 2006 and 2011. Another retrospective study conducted at the Chang Gung Hospital in Taiwan from 2011 to 2015, found 590 cases of paediatric poisoning (Lee et al., 2019). In Europe, Pawłowicz et al (2013) reported 489 children with acute poisoning in Poland during 2006 until 2010, which represents 25% of the total number of children hospitalised (Pawłowicz et al., 2013); in Spain, 1,749 cases of paediatric poisonings were obtained in a study carried out over 9 years, between 2008 and 2017 (Santiago et al., 2019) and Berta et al (2020), in Italy, observed a total of 1,030 children diagnosed with acute poisoning (2012-2017).

This introduction will exploit the literature data on the main toxic agents, routes of exposure, intents of intoxication, gender, region and age susceptibility, and finally the main measures for prevention and managing of poisoning.

1.1 Toxic Agents

A toxic agent is any chemical that, when introduced into the body, is absorbed and metabolized and causes structural or functional damage to an organ or organ system, and may include death (Calabuig, 2004). The main causes of child poisoning are pharmaceuticals products, household and/or cleaning products, diesel, toxic gases, and pesticides (Gokalp, 2019). Alcohol is also one of the most common drugs justifying admission to the emergency room (Gaw & Osterhoudt, 2019).

Pharmaceuticals

Children intoxication by pharmaceuticals is responsible for about 3–8% of the admissions to the paediatric intensive care unit (Ferranti et al., 2018). Its frequency has a bimodal distribution, peaking for children ≤ 5 years of age (at this age the possibility of long-term damage is greater due to their smaller size and less developed physiology) who are more often implicated in accidental exposure to a single medicine; and for those aged ≥13 years whose intoxication are mainly intentional (Ferranti et al., 2018; Matalová et al., 2019; Yehya et al., 2020). It must be taken into account that accidental intoxication is not only due to unintentional self-intoxication (corresponding to about 95%) but also to medicine administration errors (the remaining 5%) (Dayasiri et al., 2020).

According to data from The Centre for Toxicological Information of Prague, the majority of intoxications are due to medicines (Matalová et al., 2019). The most prevalent classes being non-steroidal anti-inflammatory drugs (NSAIDs), benzodiazepines, analgesics (including opioids and paracetamol), oral antidiabetics and antihistamines (Greene et al., 2005; Matalová et al., 2019; Yehya et al., 2020). The Toxicology Investigators Consortium from the American College of Medical Toxicology also observed high exposure to cardiovascular, antipsychotic, antidepressant, and antiepileptic drugs (Ferranti et al., 2018), highlighting a significant risk associated with cardiovascular medications, particularly calcium channel blockers, beta-blockers, and digoxin (Matalová et al., 2019; Yehya et al., 2020).

Intoxication by tricyclic antidepressants (TCAs) is common and usually intentional in adolescents and adults (Albertson et al., 2004). This class of drugs generates a large variety of clinical effects when administered in large doses (Greene et al., 2005). TCAs anticholinergic properties may delay gastric emptying causing gradual absorption. These antidepressants are metabolized by the liver, with a little portion expelled unchanged in the urine. Besides the parent drug, their active metabolites may promote poisonousness (Albertson et al., 2004). The anticholinergic effects of these medicines also include tachycardia, hot and dry skin, rapid reflexes, sedation, seizures, and urinary retention

(Albertson et al., 2004; Greene et al., 2005), tachycardia and seizures also possibly deriving from a serotoninergic syndrome. A study carried out in Turkey, from 1998 to 2004, included 44 cases of amitriptyline poisoning in children up to 14 years of age; these were more prevalent in females (52.3%) who ingested a dose ranging from 2 to 97.5 mg/kg. The most common symptoms were lethargy, tachycardia, seizures, hyperglycaemia, and leucocytosis. In this study, two children died (Caksenl et al., 2006). Kizilyidiz et al (2018) also noted that from a total of 239 paediatric poisonings between 2010 and 2011 in Turkey, 57.3% implicated pharmaceuticals. The highest incidence (29.9%) was observed for the TCAs class (Kizilyildiz et al., 2018).

Antihistamines (H1 receptor antagonists) are presented both as over the counter (OTC) and prescription only medicines. These are structurally associated to histamine and antagonize its actions at H1 receptors, being therefore applied for nausea, allergy-related itching, cough relief, flu and as sleep helpers. Drugs from this class display anticholinergic effects (except for “non-sedating” substances such as azelastine, cetirizine, desloratadine, among others) and some medicines such as diphenhydramine, have also local anaesthetic effects at high concentration. The estimated fatal oral dose of diphenhydramine is 20 to 40 mg/kg. In general, toxicity occurs after intake of 3 to 5 times the recommended daily dose, with children being more susceptible to it than adults (Albertson et al., 2004). Judge et al reported a case of diphenhydramine intoxication in a 2-year-old girl who ingested several 50-mg capsules of diphenhydramine, being initially disoriented and sleepy. At the hospital, the symptoms evolved to hallucinations, tremors and muscle spasms, being subjected to gastric lavage (Joseph Judge & Dumars Jr, 1953). Hydroxyzine was also associated as the cause of accidental poisoning in a 13-month-old female baby. The concentration detected 8.5 hours after ingestion was 102.7 µg/ml. The child had tachycardia and seizures, with full recovery within 72 hours (Magera et al., 1981).

NSAIDs are a chemically distinct class of medicines that share ident ical pharmacological characteristics and are commonly utilized to control pain and inflammation. Overdose with most of NSAIDs generates mild gastrointestinal (GI) discomfort. These drugs produce their effects (both pharmacological and toxicological) by inhibiting the cyclooxygenase enzyme (COX-1 and COX-2 isoforms), resulting in diminished production of prostaglandins and thus reduced pain and inflammation. Besides, prostaglandins preserve gastric mucosal integrity and control renal blood flow so an acute intoxication can influence these functions. Most paediatric NSAID poisonings with ibuprofen are asymptomatic when the ingested dose is less than 100 mg/kg. Symptoms for doses up to 400 mg/kg tend to appear during the first 4 hours. These include nausea, abdominal pain, and vomiting. Children have also a high risk of gastrointestinal bleeding. At higher doses

the symptoms are severe and potentially fatal. One study reported that 2 of 88 children with acute NSAID poisoning had neurological symptoms such as headache, dizziness, or seizures (Chung &Tat, 2016). A 17-year-old girl was admitted to the emergency department after a suicide attempt with ibuprofen, the serum concentration was 352 μg/ml. She had metabolic acidosis and hypothermia, underwent several treatments, but eventually died (William et al., 2007).

Ferranti et al (2018) found a 30% increase in the rate of paediatric poisonings involving anticonvulsants between 2001 and 2008 (Ferranti et al., 2018). Carbamazepine is recommended at a dose of 30-40 mg/kg/day in children ≤ 6 years of age, 600-1000 mg/day in 6-12 years and 800-1200 mg/day in those ≥ 12 years of age. Most toxic symptoms are correlated to the central nervous system (CNS) depressant effects and anticholinergic actions. Clinical signs of poisoning occur within 1 to 3 hours after intake. Though, the slow absorption rate causes a maximum serum concentration up to 24 hours, or even 70 hours after consumption in case of extended-release formulations (Albertson et al., 2004; Ferranti et al., 2018). Therapeutic and toxic blood concentrations are 6–12 μg/ml and >12 μg/ml, respectively. The manifestations of poisoning are lethargy, ataxia, dystonic reactions, nystagmus, vomiting, apnoea, and arrhythmia (Albertson et al., 2004; Ferranti et al., 2018). The 2015 Annual Report of the American Association of Poison Control Center (AAPCC) reported an increasing tendency in carbamazepine poisoning across the country, with 12.3% of cases occurring in children during 2015 (Ferranti et al., 2018). Lamotrigine is the most prescribed new-generation antiepileptic drug, being related to the greatest number of rescue interventions by virtue of its toxicity (Ferranti et al., 2018). This medicine inhibits voltage-sensitive sodium channels and blocks the release of excitatory neurotransmitters (Albertson et al., 2004). The therapeutic level is 2.5 to 15 mg/L and toxicity raises at doses above 15 mg/L. Poisoning by lamotrigine was observed in 15.3% of children in 2015, according to the 2015 Annual Report of the AAPCC (Ferranti et al., 2018). Levetiracetam, another anticonvulsant drug, is a considerable safe medicine even in poisoning cases, most intoxicated children being asymptomatic (Ferranti et al., 2018). Topiramate is recommended in a dose between 5–9 mg/kg/day in children. Although, most patients do not appear to have any toxicity signs, some may express drowsiness, lethargy, dizziness, vertigo, agitation, and confusion (Ferranti et al., 2018). According to the AAPCC 2015 Annual Report, 11.49% of valproic acid intoxications involved children. This drug is believed safe and generally well tolerated (Ferranti et al., 2018). Valproic acid enhances the synaptic amount of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) and delays the recovery of deactivated sodium channels, these actions being accountable for its activity as a CNS depressant. It also modifies the metabolism of amino acids and fatty acids, causing

hepatotoxicity, metabolic disorders, cerebral oedema and bone injury (Albertson et al., 2004). In cases of poisoning, the GI tract and CNS are the organs mainly implicated with symptoms like nausea, vomiting, abdominal pain, diarrhoea, lethargy, and drowsiness (Ferranti et al., 2018).

In children, opioid intoxications are a frequent type of life-threatening sequalae, and might cause loss of consciousness, respiratory suppression, apnoea, coma, and ultimately death (Farnaghi et al., 2021). Opiates are a class of naturally substances obtained from the poppy *Papaver Somniferum*. Morphine is the most traditional bioactive employed in medicine, while heroin (diacetylmorphine) is a semi-synthetic, highly addictive illicit drug. The term opioid is attributed to these and to other naturally extracted opium (e.g., codeine) and semisynthetic substances (e.g., hydrocodone) as well as new synthetic analogues (e.g., fentanyl, butorphanol, meperidine, methadone). This group of medicines shares the capacity to stimulate several opioid receptors in the CNS and periphery producing sedation and respiratory arrest. Apnoea or respiratory aspiration of gastric contents in children are responsible for respiratory failure, that can lead to death. Opioids maximum activity, in general, appear within 2 to 3 hours, but the absorption might be delayed by drug-induced decrease of GI motility. The clearance is very variable, from 1 to 2 hours for fentanyl metabolites, compared to 15 to 30 hours for methadone. The toxic dose also differs on the compound, route and rate of administration. Morphine potency is exceeded by some fentanyl derivatives. Mild or moderate acute intoxication tends to cause lethargy, constricted pupils, reduced pulse and blood pressure and flaccid muscles. Upon administration of great doses, coma is accompained by respiratory depression and apnoea which usually causes sudden death (Albertson et al., 2004).

Creswell et al (2019) observed that in 2016 deaths and hospital admissions from prescribed opioids accounted for 69% and 59%, respectively (Creswell et al., 2019). In 2017, there were 47,600 opioid-related deaths in the US. The highest rates occurred among individuals aged between 25 and 44 years, who are within the main periods of child parenthood. From 2009 to 2014 an estimated 2,1 million (2.9%) children aged ≤17 years were living with at least one parent with substance use disorder (Winstanley & Stover, 2019). A 29-day-old new-born died in 1998 from intoxication with codeine (used to treat cough) in Boston. The syrup contained 2 mg/ml codeine, so the therapeutic dose would be 0.63 mg/kg. However, 4 mg was administered over a 6-hour period. The symptoms consisted mainly of drowsiness but evolved to /bronchiolitis and mild bilateral pulmonary congestion (Magnani & Evans, 1999).

Tramadol is an opioid analgesic applied to treat moderate or acute pain. Intoxication by this drug cause long-term hospitalization in approximately 10% of patients. It acts as a partial agonist in μ-opioid receptors and inhibits serotonin reuptake (Albertson et al., 2004; Goudarzi et al., 2020); both these mechanisms contribute to analgesia. Goudarzi et al (2020) identified 189 patients aged ≤18 years with tramadol intoxication between 2010 and 2015; of these, 93.1% related to intentional cases. Users were also asked about the availability of the drug; 62.4% reported that the product was already available at home and 36.5% of patients bought tramadol at a pharmacy without a prescription (Goudarzi et al., 2020). Although adults are the biggest consumers of opioids, this problem also affects children and adolescents as the growth in their prescription results in larger availability of these medicines (Creswell et al., 2019; Franchitto, 2020; Winstanley & Stover, 2019). Some intoxication studies show a bimodal distribution regarding age, where young children (< 6 years) and teenagers (≥ 13 years) are the mainly exposed to opioids (Creswell et al., 2019; Franchitto, 2020). Accidental exposure mainly occurs in toddlers as they tend to explore the environment with hand-to-mouth movements and are easily exposed to inadequately stored household products and medicines. In addition, they mimick the behaviour of adults (Farnaghi et al., 2021; Franchitto, 2020).

The increase in opioid prescription has been accompanied by escalating rates of individuals initiating treatment for Opioid Use Disorder (OUD) (Creswell et al., 2019; Farnaghi et al., 2021; Winstanley & Stover, 2019). The current epidemic of these medicines in the US has caused an expansion in the number of accidental and voluntary poisonings (Creswell et al., 2019). Methadone and buprenorphine are the drugs approved by the US Food and Drug Administration for the treatment of OUD (Farnaghi et al., 2021; Winstanley & Stover, 2019). Buprenorphine is a partial μ receptor agonist and κ antagonist, synthesized as an alternative to morphine but with fewer side effects. It is available in medicines with dosages from 0.2 to 8 mg, being mainly presented in the form of orodispersible tablets. Compared with methadone, buprenorphine produces less severe opioid syndrome and do not cause less respiratory depression. Buprenorphine poisoning in children ≤ 6 years is more serious, with 48.1% of exposed children needing to be hospitalized and 21.4% displaying a severe medical outcome (Farnaghi et al., 2021; Franchitto, 2020; von Fabeck et al., 2020). Between 2000 and 2015, from the 188,468 reports from various poison control centers in USA, buprenorphine was involved in 3.3% (Winstanley & Stover, 2019). Regarding to methadone toxicity in children, Alotaibi et al. (2012) found that exposure led to critical intoxications as even ingestion of small quantities were lethal in this age group (Alotaibi et al., 2012) In a study carried out in children up to 12 years of age admitted to the hospital in Tehran between 2018 and 2019, 120 patients were diagnosed with accidental

poisoning by methadone (in tablets or syrup) or buprenorphine (sublingual). More intoxication cases implicated methadone, compared to buprenorphine, which can be attributed to the greater exposure to this drug in general population (Farnaghi et al., 2021).

Tranquilizers, sedatives and hypnotics are also widely used medicines for the treatment of various psychological issues, including anxiety disorders and insomnia (Geulayov et al., 2018). Coben et al (2010) noted that this class (diazepam, alprazolam, phenobarbital) has contributed to an increase in deaths, 1999 to 2004, from accidental poisoning (Coben et al., 2010).

Benzodiazepines are a broad group of sedative-hypnotic medicines related with a lot of emergency room accesses (Ferranti et al., 2018). This class contains several substances that differ in potency, duration of action, presence or absence of active metabolites, and their clinical application. Benzodiazepines increase the activity of the inhibitory neurotransmitter GABA and block other neuronal structures through processes that are still weakly studied. The consequence is a widespread depression of spinal reflexes and the reticular activating system, which can lead to coma and respiratory arrest (Albertson et al., 2004). After ingestion most drugs of the group are metabolised into active metabolites which suffer enterohepatic circulation (Ferranti et al., 2018). Intoxication sings involve drowsiness, confusion, agitation, hallucinations, ataxia, and occasionally, respiratory and cardiac depression (Albertson et al., 2004; Ferranti et al., 2018). Death from poisoning is not frequent, except when combined with other CNS depressant agents such as ethanol or barbiturates (Albertson et al., 2004; Ferranti et al., 2018).

The Multicenter Study of Self-harm in England showed that 79% of all hospital admissions to the emergency department are due to intentional poisoning and 14% of these involve benzodiazepines/hypnotics. Geulayov et al (2018) detected 179 suicides in individuals aged ≥ 15 years due to benzodiazepine/hypnotic intoxication. In 5% of these patients, at least one of these medicines would have been prescribed, with diazepam being the most prescribed drug, followed by zopiclone and zolpidem. In addition, they also observed an average of 576 non-fatal hospital admissions per year involving this group of drugs (Geulayov et al., 2018).

Products used for flu and cough are also associated with childhood poisoning (Berta et al., 2020; Hoikka et al., 2013; Koh et al., 2018). Dextromethorphan is an antitussive medicine found in numerous cough and flu preparations. Although severe poisoning is rare, it still occurs with some frequency in children. This active ingredient is a synthetic analogue of codeine not showing analgesic or additive characteristics. In overdose, it generates mild opioid effects. The *N*-methyl-*D*-aspartate (NMDA) glutamate receptors are antagonized by

both dextromethorphan and its *o*-demethylated metabolite. When dextromethorphan is taken in a single dose above 10 mg/kg it frequently results in symptoms of intoxication. The suggested daily dose for children aged 2 to 5 years is up to 30 mg/day. Mild poisoning causes dizziness, ataxia, nystagmus, mydriasis, and restlessness (Albertson et al., 2004). A study in Cincinnati Poison Control Center, during year 2010, observed that 71% of the cases involved voluntary abuse of dextromethorphan and 85% of patients were 13 to 17 years old (Banerji et al., 2001). Fern & Graudins (1996) reported a case of an 8-year-old boy with an overdose of dextromethorphan, whose main signs were extreme drowsiness and involuntary muscle contractions. He remained for 6 hours in the emergency room, with subsequent discharge (Graudins & Fern, 1996).

Table 1- Studies on pharmaceutical involved in paediatric poisoning

Reference	Study period	Age group	Total intoxication cases	Sex	Cases involving pharmaceuticals	Most common toxicants	Other relevant information
Dayasiri et al (2020)	2007-2014	9 months to 12 years	1621	185 females (45.1%) 225 females (54.9%)	410 (25.3%)	Analgesics Anticonvulsants Antiasthmatics	7 children (59.8%) belonged to the 3–5 years age
Matalová et al (2019)	2010-2012	≤18 years	15069	40 females (72.3%) 10 males (27.3%)	55 (0.36%)	Paracetamol Ibuprofen Dimetindene Clonazepam	Girls were prevalent in adolescence Intentional: 41.8% Suicide attempt: 32.7% of the intentional cases Accidental: 58.2%
K.Von Fabeck et al (2020)	2009-2018	≤18 years	54	29 females (53.7%) 25 males (46.3%)	54	Buprenorphine	Unintentional: 52 Therapeutic error: 2
Creswell et al (2019)	2002-2016	≤19 years	2.725	1476 females (54.2%) 1249 males (45.8%)	2.725	Opioids	Intentional: 395 Suicide attempt:353 Accidental:1874 Therapeutic error- 613.
Ahmadi et al (2010)	2006-2008	All ages (15.1% children from 6 to 17 years old)	2.057	1108 females (53.9%) 949 males (46.1%)	1598 (77.7%)	Benzodiazepines Opioids Other medicines	1.748 (85%) intentional intoxication cases. 1.022 (58.4%) being females
Nistor et al (2016)	2014	10-19 years	219	103 females (47%) 116 males (53%)	76 (18 (15.5%) males and 58 (56.3%) females)	Paracetamol Benzodiazepines Antiepileptics	Self-poisoning: 34.7% of total cases. mainly in girls 56.3%. All the cases were intentional
Azab et al (2016)	2009-2013	≤18 years	38.470	21.522 females (55.9%) 16.948 males (44.1%)	15.468 (40.2%)	Non-opioid analgesics Antipyretics Antirheumatics	Male - accidental poisoning (85.8% vs. 54.9%); Female- intentional poisoning (44.7% vs. 10.2%). Unintentional intoxication on preschool and school groups -99.6%. Self-harm intent in adolescents- 84.1%
Ulseth et al (2022)	2014-2015	13-18 years	68	48 females (71%) 20 males (29%)	29 (43%)	Paracetamol was the most common	Deliberate self-harm: 32 Substance misuse-related poisoning:35. Girls accounted for 24 out of 29 poisonings involving medications alone.
Lee et al (2019)	2011-2015	≤18 years	590	281 females (47.7%) 309 males (52.3%)	244 (41.4%)	Hypnotics and sedatives Antipsychotics Antidepressants Anticonvulsants	All cases ≤11 years were boys (53.3%); Cases ≥11 years were mainly girls (53.1%). Children ≤ 5 years were associated with accidental intoxication. Pharmaceuticals were used in 26 intentional cases
Lamireau et al (2002)	1989-1995	≤18 years	2.643	Higher rate among boys	1386	Benzodiazepines Paracetamol Antihistamines	80% of the patients were ≤4 years and 57% were boys. Between 12-15 years. females predominated (65%)
Pac-Kozuchowska et al (2016)	2008-2012	≤18 years	848	439 females (51.77%) 409 males (48.23%)	348 (58.97%)	Analgesics Antiepileptics Respiratory system medications Psychotropics	Females form urban areas were more prevalent (53%); From the study population 45.17% were children's ≤5 years and 40% were 14-15-year-old females Accidental- 56.01% Intentional- 43.99%

Alcohol

Acute alcohol intoxication consists in a medical condition caused by a recent consumption of ethanol, arising from the rapid accumulation of the parent drug and its metabolites in the bloodstream by virtue of the inability of the body to timely perform their detoxification. Alcohol consumption by adolescents is one of the Europe's major social problems and it can produce a range of immediate and late effects (Pawłowska-Kamieniak et al., 2018; Rodrigues et al., 2018). Pianca et al (2017) reported that approximately 15% of users aged ≥15 experienced episodes of excessive alcohol consumption (*i.e.*, binge drinking) (Pianca et al., 2017).

Ethanol is fast absorbed from the GI tract and is toxic to the body due to its main pharmacodynamic mechanism which consists of increasing inhibitory transmission of GABA. This effect is produced both by ethanol and by its main metabolite, acetic aldehyde (Pawłowska-Kamieniak et al., 2018; Pianca et al., 2017). Ethanol is highly hydrophilic and has greater volume of distribution in young children due to their higher body water content, compared adults. Therefore, they may display smaller blood alcohol concentration (BAC). The absorption of ethanol and its following distribution to the several tissues in infants originate atypical clinical symptoms. Ethanol metabolism starts with the oxidation of ethanol to acetaldehyde by various enzymatic systems, such as alcohol dehydrogenase (ADH) – the preferential pathway at low BAC, cytochrome P450 (isoform CYP2E1) and catalase.

Thus, 90% of the absorbed ethanol is metabolized hepatically by oxidation at a standard rate of 15 mg/dl per hour. Therefore, ingestion that goes beyond this rate can induces poisoning symptoms (Jung & Namkoong, 2014). In young children, ADH activity is inferior to adults; therefore, alcohol is alternatively metabolized by other pathways such as CYP2E1 and to a lesser extent catalase. The excretion of ethanol occurs primarily through metabolism; various studies have reported elimination rates twice as fast as adults, while others describe identical elimination rates (Gaw & Osterhoudt, 2019). Furthermore, young children exposed to ethanol are hypothetically at a larger risk of hypoglycaemia due to the lower amount of stored liver glycogen. The same can happen for teenagers. Other metabolic effects that can occur are acidosis, hypokalaemia, hypomagnesemia, and hypophosphatemia (Gaw & Osterhoudt, 2019; Pianca et al., 2017).

The signs of acute alcohol poisoning are dose-dependent, that is, they are associated to the drug serum level. Still, there is also the influence of individual susceptibility, such as age, gender and type and number of alcoholic beverages consumed (Pawłowska-Kamieniak et al., 2018; Pianca et al., 2017). The most common symptoms are mood/behaviour alterations, slurred speech, lack of coordination, unsteady gait, nystagmus,

attention or memory insufficiency and, in more serious cases, coma. It should be highlighted that the impact on the level of consciousness according to the BAC, vary from mild sedation to coma (Pianca et al., 2017).

The total of children and young people who seek alcoholic drinks continues to increase, both in rural and urban environments, according to Pawlowska-Kamieniak et al (2018) (Pawłowska-Kamieniak et al., 2018). Adolescence is associated with a greater probability of intentional intoxication, due to a growing phenomenon called binge drinking – whose objective is the ingestion of huge amounts of alcohol in a short period of time. This is related to the need to call attention from the family, or peers' environment (Pawłowska-Kamieniak et al., 2018; Pianca et al., 2017). Binge drinking, according to the National Institute on Alcohol Abuse and Alcoholism from USA, corresponds to the consumption of enough alcohol to raise the BAC to 8 mg, which corresponds to at least five drinks in men and four drinks in women within two hours (i.e., an episode of rapid ingestion) (Schulte et al., 2009).

Alcohol intoxication in young children typically results from accidental ingestion or a pathological effect of intra-family relationships, such as mimicking parental behaviour (Gaw & Osterhoudt, 2019; Pawłowska-Kamieniak et al., 2018). This is due to the omnipresent nature of ethanol. Ethanol is present in beer, wine and spirits, household products and pharmaceutical products, but also in cooking wines, flavour extracts and fermented foods. Still non-alcoholic foods, such as bread, yogurts, and fruit juices, are also likely to contain little quantities of this compound. Given its usefulness as an antiseptic and organic solvent, ethanol can be also found in countless household products, including cosmetics, personal care and cleaning products such as perfumes, colognes, mouthwashes and hand sanitizers. Ethanol is still used as an excipient in medicines, mainly in liquid formulations, which may represent up to 10% (v/v). Combining children's exploratory behaviour, characteristic of development, to the fact that they perceive alcoholic drinks like gin or vodka as water, makes them susceptible to alcoholic intoxication. Even so, this age group may be subject to intentional actions by parents not only for alcohol medicinal use (rubbing on babies' gums to relieve toothache), but also for the malicious administration in cases of abuse or neglect (Gaw & Osterhoudt, 2019).

Schulte et al (2009) described some risk and protective factors that contribute to alcohol intoxication in adolescence. Social environment affects consumption through proximal and distal experiences of peer behaviour. For example, association with a deviant group offers more chances to drink and/or seeing drinking as a way of dealing with stress or for having fun. Alcohol can be used as a coping tactic by teens because of the lower

parental monitoring that is related to emotional dysregulation in a deviant peer network. In addition, the education style – with attention and discipline – suggests that young people have a greater ability to resist the social pressure of alcohol consumption. However, boys may consider this style as challenging (Schulte et al., 2009).

There are gender differences in alcohol consumption and its intoxication. Therefore, some factors, mentioned below, lead to a lower alcohol consumption by women, such as women's physical sensitivity to smaller doses, more social inhibition and sanctions in some cultures, and enhanced risk of physical and sexual aggression. Gender distinction is also observed by parental influence on alcohol consumption by adolescents, since boys may be directly persuaded by their parents' consumption, compared to girls. In addition, cultural norms differ between girls and boys in terms of supervision and punishment. Females are more protected, while boys have more freedom to interact with peers who instruct and emphasize alcohol use. In fact, attitudes and beliefs about the acceptability of drinking are affected by traditional gender roles ideas, such as the case that men drink more frequently than women to demonstrate their masculinity. On the other hand, girls and women who follow stereotyped female qualities (virtue, affection, and emotionality) tend to report less involvement with alcohol. Adolescents' attitudes regarding traditional gender roles significantly mediate the connection between gender and consumption patterns, with larger mediation effects for intoxication (Schulte et al., 2009). The media also affect peer perceptions of alcohol use, which tends to influence expectations about gender roles and the relationship of these to drinking. The constant message that connects masculinity to drinking and intoxication is repeated by several sources. Thus, gender-specific actions are frequently reinforced for boys, getting them reliable predictors of alcohol use as they progress across puberty (Schulte et al., 2009).

Table 2- Studies on alcohol involved in paediatric poisoning

Reference	Study period	Age group	Total intoxication cases	Sex	Cases involving alcohol	BAC	Other relevant information
Pawłowska-Kamieniak et al (2018)	2004-2013	≤18 years	402	172 females 230 males	402	0.1-3.9‰	More prevalent in urban children's
Rodrigues et al (2018)	2012-2016	10-17 years	180	63 females (35%) 117 males (65%)	180	1.0-3.0‰	More common in boys. mostly in parties
Oliveira et al (2011)	2003-2007	≤18 years	338	119 females (35.2%) 219 males (64.8%)	338	-	Alcohol cases: 64.8% male
Ulseth et al (2022)	2014-2015	13-18 years	68	48 females (71%) 20 males (29%)	26 (38%)	-	Deliberate self-harm: 32 Substance misuse-related poisoning: 35 Alcohol cases more prevalent in males
Nistor et al (2016)	2014	10-19 years	219	103 females (47%) 116 males (53%)	71 (55 (47.4%) males; 16 (15.5%) females)	Average inboys:3‰ and girls: 2.5‰	Alcohol cases more prevalent in males
Pawłowicz et al (2014)	2006-2010	≤18 years	489	233 females (47.6%) 256 males (52.4%)	244 (49.9%)	-	Intentional: 369 Accidental: 120 In adolescents. alcohol cases were more prevalent in males. 356 intentional alcohol intoxications in the 13-18 years group
Pac-Kozuchowska et al (2016)	2008-2012	≤18 years	848	439 females (51.77%) 409 males (48.23%)	217 (25%)	-	In children < 6 years. alcohol was the most frequent cause for intoxication.
Bouthoorn et al (2011)	2007-2009	11-17 years	800	391 females 409 males	800	Average in boys-1.94‰ and girls-1.79 ‰	Higher prevalence of alcohol intoxication in in 16-year-old boys (32.5%) and 15-year-old girls (29.2%). Intoxicated girls had a lower BAC than boys.
Kaminska et al (2018)	2000-2011	≤18 years	227	108 females (47.6%) 119 males (52.4%)	250 (2.8%). Only 227 reports were obtained	Mean BAC: 1.55 ‰	Hospitalizations constituted 28% of all urgent admissions. 99 children between 14 to 16 years were hospitalized due to alcohol intoxication.
Woolfen et al (2002)	1996-2000	10-18 years	212	100 females (47%) 112 males (53%)	212	-	49 children were ≤14r. The greatest number of intoxications occurred on weekend (46%) and friday (18%).
Bitunjac et al (2009)	1997-2007	≤18 years	594	69 females (28.9%) 170 boys (71.1%)	239 (40.2%)	-	82% of intoxications occurred in the group 14-18 years. 175 children were hospitalized (73.2%) on weekends due to alcohol intoxication
Kuzelová et al (2009)	1996-2005	≤18 years	537	264 females (49%) 273 males (51%)	537	1.98 g/L	All intoxications were intentional. The greatest BAC (4.39 g/L) was found in a 17-year-old boy.

Illicit Drugs

Poisoning by illicit drugs is barely observed in paediatric emergency units, representing approximately 1.5% of all cases of intoxication in Spain (Azkunaga et al., 2017). These are usually unintentional in little children who have an exploratory behaviour, appropriate for their age. However, in teens the use is intentional. The Toxicological Surveillance System of the Spanish Society of Paediatric Emergency, observed 1,139 paediatric intoxications, 32 (2.8%) of which were related to illicit drugs (Azkunaga et al., 2017).

The most administered illicit drug in USA is cannabis, derived from the *Cannabis sativa* (Wong & Baum, 2019). The products of this plant have many forms like marijuana (dried, crushed flower heads and leaves), hashish (resin) and hashish oil (concentrated resin extract) and might be smoked, inhaled, or ingested (Chen & Klig, 2019; Wong & Baum, 2019). Marijuana is more often smoked in cigarettes or pipes but can also be put into food (normally cookies or brownies) (Albertson et al., 2004). Cannabis has over 500 chemical elements known as phytocannabinoids, which act on specific receptors in the CNS and the immune system. The best-known cannabinoids are delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD), the former being the main psychotropic substance in the plant, accounting for most signs of CNS intoxication, in contrast to CBD, which is non psychoactive (Albertson et al., 2004; Wong & Baum, 2019). The potency of the drug is established on its THC level. This compound is fat-soluble and has a great affinity for proteins, having a volume of distribution of 2.5 to 3.5 L/kg (Wong & Baum, 2019). The stimulant, hallucinogenic or sedative effects are produced by THC, when it attaches to cannabinoid receptors presents in the brain (dose- and time-dependent) (Albertson et al., 2004; Wong & Baum, 2019). This element has direct activity on the endocannabinoid system and indirectly on the glutamatergic, GABAergic, and dopaminergic system. Endocannabinoid receptors (CB-1 and CB-2) exist in elevated concentrations in the frontal and limbic regions of the cortex, hippocampus, amygdala, cerebellum, thalamus, and basal ganglia (Chen & Klig, 2019). Binding of the compound to the receptor will cause cognitive and motor impairment (Wong & Baum, 2019). It can be also seen a block of sympathetic reflexes (causing orthostatic hypotension) and a catecholamine release (producing tachycardia) (Albertson et al., 2004). A teenager's brain has a larger number of cannabinoid receptors and consequently tends to be more susceptible to the effects of THC (Chen & Klig, 2019).

The symptoms can be neurological (euphoria, disorientation, pleasurable sensations, and others), ophthalmologic (dilated and sluggish pupils), cardiovascular (tachycardia) and GI (nausea, vomiting, increased appetite, or thirst) (Pianca et al., 2017;

Wong & Baum, 2019). Yet, the most prevalent symptom in child ≤3 years is neurological impairment, in contrast to what occurs in adults and older children (Claudet et al., 2017).

Unintentional cannabis intoxication represents a major health problem, as many countries have already decriminalized, legalized, or authorized the consumption of marijuana for medical reasons, which caused an increase in paediatric intake (Claudet et al., 2017). This growth is likely multifactorial: high availability, multiple modes of delivery and better cannabis palatability. Last years, the potency of items containing cannabis has grown significantly, i.e., the concentration of THC in the resin or leaf is higher, which may clarify the more severe poisonings identified despite relatively small intakes, especially in younger children (Claudet et al., 2017; Wong & Baum, 2019).

The most frequent place of accidental exposure in kids is in home, through the edible form. Products of this genre are very attractive and easily ingested, as cookies, brownies, chocolate bars and gummies, in addition to being identical to various types of sweets known to children (Chen & Klig, 2019; Wong & Baum, 2019). There are also cases where the toxicity is due to parent administration of hemp oil supplements, as THC is present in tiny amounts. Intoxication can usually occur within 30 minutes to 3 hours (Chen & Klig, 2019).

Cannabis is the most common substance used by teenagers in the US. The edible form is becoming increasingly popular because it is like regular food. Forms of hashish or marijuana are often smokable mixed with tobacco (Chen & Klig, 2019). The use of this drug can lead to physical injuries, since ingestion can decrease cognitive, perceptual, and psychomotor function. Most injuries are accidental like falls or road accidents. In adolescents, cannabis poisoning impacts they judgment causing risk behaviours (Chen & Klig, 2019).

Wang et al (2014) reported that intakes in children ≤10 years increased from 1.2 to 2.3 per 100,000 population with decriminalization, and that emergency room visits among adolescents increased from 1.8 to 4.9 per 1,000 visits in the Colorado between 2009 and 2015 (Wang, 2014). A study carried out for 10 years (2004-2014) in children ≤3 years in France found 29 cases of accidental cannabis intoxication (Claudet et al., 2017).

Cocaine children intoxication is a global health problem, leading to many medical complications from morbidity to death (Albertson et al., 2004; Zimmerman, 2012). Cocaine users in the US ≥ 12 years totalled 1.5 million in 2010. The use of this illicit drug has been increasing in Europe, following cannabis (Zimmerman, 2012). Cocaine (benzoylmethylecgonine) is extracted from the leaves of the *Erythroxylon coca* plant by immersing the leaves in organic solvents to form a thick paste sediment. The addition of hydrochloric acid to the paste results in the precipitation of the salt, which consists in a white

powder. This form of cocaine is water soluble, so it can be injected, inhaled, or ingested. In addition, the consolidation of salt, through the addition of a base (sodium bicarbonate) to its alkaloid form, with subsequent drying, a process called “free-basing”, can be smoked, giving it the name of Crack (Albertson et al., 2004; Ryan, 2019; Zimmerman, 2012).

This illicit drug is absorbed through the oral and nasal mucosa, as well as through the respiratory, GI, and genitourinary tracts. Thus, after ingestion, its distribution and absorption occur by most organs, including the brain, heart, kidney, adrenal glands, and liver (Albertson et al., 2004; Ryan, 2019). Cocaine produces local anaesthetic, vasoconstrictor and sympathomimetic effects (Albertson et al., 2004; Zimmerman, 2012). The sympathomimetic action of cocaine is responsible for poisoning, whereas inhibits the presynaptic reuptake of biogenic amines, such as norepinephrine, dopamine, and serotonin, throughout the body, including the CNS, which produces an increase in extracellular and synaptic levels of these neurotransmitters. The mesolimbic dopaminergic pathway, which includes brain structures for reward processing, impulse control and inhibition and the neurotransmitters, dominates the psychotropic and addictive effect of cocaine. This causes a rise in heart rate and blood pressure with diffuse vasoconstriction; acute euphoria and self-confidence at lower doses and agitation and delirium at higher doses (Albertson et al., 2004; Ryan, 2019; Zimmerman, 2012).

The physiological effects of cocaine vary according to the route of administration, the form of cocaine and the concomitant use of other drugs. Onset of effects is faster with inhaled cocaine (3-5 seconds) but the duration of effects is longer with intranasal use (60 to 90 minutes). The short duration often leads to repeated doses being taken to maintain desired effects (Ryan, 2019; Zimmerman, 2012).

The desired effect of cocaine use is euphoria, adding to experiencing increased energy, alertness, and sociability, decreased appetite and need for sleep. With improving duration of use, higher doses or more efficient routes of administration, individuals may experience dysphoric effects such as anxiety, irritability, restlessness, and agitation (Ryan, 2019). Acute intoxication manifests with tachycardia, hypertension and agitation. Additional findings often include mydriasis, sweating, hyperthermia, and tachypnoea. In relation to the CNS, paranoia and severe delirium can be observed. (Albertson et al., 2004; Zimmerman, 2012).

Cocaine use occurs in all demographic and socioeconomic groups. Results from the 2017 National Survey on the Use of Medicines for Health in USA indicated that about 0.1% of 12 to 17 years old (about 26,000 individuals) and 1.9% of 18- to 25-year-olds (about 665,000 individuals) were currently using cocaine (Ryan, 2019). A 9-month-old boy

presented at the Wisconsin hospital with no response, rapid breathing, and moaning, obtain the diagnosis of cocaine intoxication in 1998. It and its metabolites were detected in urine at a concentration of 0.19 mg/L and 2.36 mg/L, respectively (Garland et al., 1989). Mott et al (1994) observed 41 cases of children up to 18 years of age, during a period of 1 year (1994), with a diagnosis of cocaine intoxication in USA. These report a pattern relating age to symptoms: in children younger than 5 years - seizures and drowsiness and in older children (≥8 years) - delirium, lethargy, dizziness, and drooling (Mott et al., 1994).

Novel Psychoactive Substances (NPS) consist of recent synthetic illicit drugs, or analogues of common illicit drugs, that may be more potent, as well as more challenging to identify and detect. Despite the lack of accurate epidemiological data, these substances are a public health problem that affects teenagers. These are often labelled as *designer drugs, research chemicals, legal highs, or psychoactive substances* (Wang & Hoyte, 2019). Despite the US Drug Enforcement Administration has made the distribution and consumption of these drugs illegal, drug manufacturers and distributors have circumvented this by selling them as legal or non-drug products, such as incense, plant foods or bath salts; being labelled “Not for Human Consumption” or “For Use in Research Only” to avoid liability for abuse or misuse (Wang & Hoyte, 2019). Access to NPS is quite easy because they are produced outside Europe and can be purchased from online stores, specialty stores and even the illegal drug market (Krakowiak et al., 2020).

The developed chemical is like other illicit drugs, with slight changes in its chemical structure, making its identification tricky since standard urine immunoassays for drug detection are not able to recognize NPS. These structural changes also produce different physiological responses and medical signs (Wang & Hoyte, 2019). Medical signs described in the literature involve agitation, increased heart rate, nausea, vomiting, insomnia, urinary retention, hallucinations, and psychedelic symptoms (Krakowiak et al., 2020).

Synthetic cannabinoids are chemically synthesized analogues of natural cannabinoids. These are sold in powder or spray form or mixed to marijuana, dried herbs/plants or other hallucinogenic plants. They are frequently called *K2, Spice or Buddha*. In 2010, more than 11,000 cases admitted to the emergency room, at Colorado hospital, were associated with these compounds, with a prevalence of 75% in adolescents and young adults aged 12 to 29 years (Wang & Hoyte, 2019). In the USA, there were 3,780 and 7,584 visits to the emergency department in 2010 and 2011 due to poisoning by synthetic cannabinoids in adolescents (between 12 and 17 years old) (Warrick et al., 2017).

Phencyclidine (PCP), ketamine and analogues are arylcyclohexamines that show their dissociative effects by antagonizing N-methyl-D-aspartate receptors (Wang & Hoyte,

2019). Both create a generalized loss of pain perception with small or no depression of airway reflexes or ventilation. They are usually smoked, but can also be inhaled, ingested or injected. The duration of the effects of PCP after an overdose is very variable and differs from 11 to 14 hours or from 1 to 4 days. Ketamine has effects that last from 30 minutes to 2 hours (Albertson et al., 2004). The American Substance Abuse and Mental Health Services Administration reported that 2.5% of adolescents and young adults over 12 years of age have used PCP in their lifetime (Wang & Hoyte, 2019). 6 cases of PCP poisoning were diagnosed in children ≤ 5 years in Los Angeles between 1978 and 1980. The main signs were lethargy, strange behaviour and staring eyes. Of these cases, 4 were male and 2 were female, and all recover between 48 and 72 hours (Welch & Correa, 1980).

Lysergic acid diethylamide, called LSD, has been misused for some years due to its hallucinogenic characteristics. LSD and its analogues are usually utilized in the form of a powder or blotter orally or sublingually (Wang & Hoyte, 2019). Its clinical manifestations occur because of the activation of the serotoninergic receptor, corresponding to hallucinations, euphoria, tachycardia, and hypertension. Some of the side effects such as anxiety, psychosis, dilated pupils, kidney injury, hyperthermia, and seizures happen by the stimulation of central and peripheral sympathetic system (Albertson et al., 2004; Wang & Hoyte, 2019). Paranoia or panic attacks can appear with any dose, but this sign lean on the environment and the patient's present emotional status (Albertson et al., 2004). LSD analogues have a similar onset of action but produce less euphoria and fewer effects compared to LSD. The Monitoring the Future of USA reports that less than 3% of all 8ths, 10th, and 12th graders confessed the use of LSD during 2017 (Wang & Hoyte, 2019). In 1971, Sweden, a 2-year-old boy ingested 5 tablets (each with 0.4 mg of LSD) which resulted in a state of high excitability, ataxia, tachycardia, and mydriasis. A gastric lavage was performed to remove the entire amount of the drug, without any sequelae Samuelsson, 1974).

3,4-Methylenedioxymethamphetamine (MDMA), popularly known as ecstasy, is a substance consumed on a large scale in the population, being associated with potentially fatal complications (Pianca et al., 2017). Although it is present in the form of coloured tablets, similar to candy, and therefore a source of attraction for children, few cases of poisoning in toddlers are reported (Eifinger et al., 2008; Pauwels et al., 2013). This compound corresponds to a methamphetamine structurally related to hallucinogenic substances, such as mescaline, amphetamine and monoaminergic neurotransmitters (Fonseca et al., 2021). CYP2D6 is primarily responsible for the metabolism of MDMA in the liver (Eifinger et al., 2008; Fonseca et al., 2021). However, this drug has auto-inhibitory properties, by preventing the action of the CYP2D6 isoenzyme, decreasing its own

metabolism. So, high plasma concentrations of MDMA and/or its metabolites can cause serious damage to the body (Fonseca et al., 2021). The $T^{1/2}$ is around 8-9 h, regardless of dose, with a maximum effect 2 hours after consumption (Fonseca et al., 2021; Pauwels et al., 2013; Pianca et al., 2017). But, according to Eifinger et al (2008), this is approximately 6.1 hours in young children (Eifinger et al., 2008).

Ecstasy acts as an inhibitor of monoamine reuptake, particularly serotonin, but also norepinephrine and dopamine, interacting with their transporters. Thus, is an indirect sympathomimetic. Inhibition of serotonin reuptake is believed to be responsible for its mood altering and psychomotor agitation (Eifinger et al., 2008; Fonseca et al., 2021; Pauwels et al., 2013). The acute effects of MDMA intoxication are a combination of hallucinogenic and stimulant manifestations. The physiological effects consist of hyperthermia, hypertension, tachycardia, sweating, muscle tension, insomnia, among others. In addition, an increase in the perception of colours and sounds, panic attacks and psychosis can happen (Eifinger et al., 2008; Pianca et al., 2017).

Eifinger et al (2008) mentioned that, until 2007, only 8 reports of ecstasy intoxication in children (5 boys and 3 girls) were published in the past decade (Eifinger et al., 2008). A 14-month-old boy swallowed part of an MDMA pill, presented to a hospital in Tenerife in 2004 with hypothermia, tachycardia, tachypnoea and mydriasis. The analyses showed an amount of 0.591 mg/L of ecstasy (Melian et al., 2004). Rijswijk et al (2006) reported a accidental poisoning in an 8-month-old child who ingested 2 or 3 MDMA pills in 2003 (Tel Aviv). Within 30 minutes, rapid breathing, excessive sweating, and adrenergic symptoms were observed. The concentrations found in blood and urine were less than 50 µg/L and 800 µg/L, respectively. Also, MDMA intoxication in children aged 24 and 11 months, whose symptoms were similar and who survived, are also described in the literature (Rijswijk et al., 2006).

Table 3- Studies on illicit drugs involved in paediatric poisoning

Reference	Study period	Age group	Total intoxication cases	Sex	Cases involving illicit drugs	Other relevant information
Gokalp, Gamze (2019)	2017	≤18 years	453	202 females (46.4%) 233 males (53.6%)	12 (2.6%)	Suicide attempt mainly occurs in females (37 vs 10) and accidental poisoning in males (233 vs 165)
Nistor et al (2016)	2014	10-19 years	219	103 females (47%) 116 males (53%)	45 (36 (31%) males and 9 females (8.7%))	Mostly cannabis and more prevalent in boys
Pac-Kozuchowska et al (2016)	2008-2012	≤18 years	848	439 females (51.77%) 409 males (48.23%)	39 (4.6%)	More often involved in urban poisoning incidents (5.3%) than rural (3.3%). Occurred mostly in teens (89.5%).
Krakowiak et al (2020)	2008-2013	All ages	576	99 females (17,2%) 477 males (82.8%)	158 (27.4%) (school or college students)	Only NPS
Claudet et al (2017)	2004-2014	≤ 3 years	29	-	29 (cannabis only)	The median age was 15,1 months. 69% of the cases were due to resin, followed by grass (2) and cake (1).
Ulseth et al (2022)	2014-2015	13-18 years	68	48 females (71%) 20 males (29%)	< 5 (7.3%)	Deliberate self-harm: 32 Substance misuse-related poisoning: 35
Pawłowicz et al (2014)	2006-2010	≤18 years	489	233 females (47%) 256 males (52.4%)	23 (4.7%)	Mostly NPS, cannabis and amphetamine. The gender distribution was equal.
Mintegi et al (2006)	2001-2002	≤19 years	2.157	-	33 (1.5%)	Children ≤ 14 years were more prevalent (17), followed by children ≥ 6 years (12). Intoxication episodes occurred at weekends.
Graham et al (2020)	2006-2016	<10 years	9122	4378 females (48%) 4743 males (52%)	9122	Most of the intoxications happen in the group from 1 to 2 years old. Marijuana (3365) and Methamphetamine (2752) were the most commonly toxics. 7926 intoxications were unintentional. Drowsiness and lethargy were prevalent (23%).
Oral et al (2011)	2004-2008	<5 years	232	109 females (47%) 123 males (53%)	232	All intoxications included alleged maltreatment: 129 physical abuses, 83 neglect and 20 sexual abuse. Multiple symptoms were present in 106 cases. Most of the children were male.
Patrick et al (2019)	2007-2017	10-18 years	49757 calls	18.113 females (36%) 31.644 (64%) boys	49757 calls	Marijuana (18216) and synthetic cannabinoids (10586) were the illicit drugs more common. 90-97% of the children went to a healthcare service. The symptoms were most severe in LSD (1881), synthetic cathinone's (840) and heroin (1047).

Pesticides

Pesticides are a wide classification of chemicals that are employed to kill or manage unwanted insects, plants, fungi or animals (e.g., rodents) (Detsouli et al., 2017; Roberts et al., 2012). Pesticides poisoning is considered a major public health hazard worldwide (Detsouli et al., 2017).

Children are especially vulnerable to the absorption and adverse effects of pesticides due to developmental, nutritional and physical factors. Therefore, accidental ingestion by kids may involve a significantly higher dose than an adult due to the fact that the ingested dose is higher per kilogram of body weight. Exposure occurs by ingestion, inhalation or dermal contact. Children demonstrate regular hand-to-mouth action, and this is a crucial source of pesticide exposure compared to adults. Thus, the use of pesticides in the home and gardens poses a risk of poisoning as they have this typical exploratory behaviour, such as playing and dragging on the floor (Roberts et al., 2012). In addition, these products may be stored in inappropriate places or misused by adults (Detsouli et al., 2017).

Paraquat is one of the largest commonly used herbicides, holding the highest rate of the global herbicide market until, recently, being overpast by glyphosate. As it is highly toxic to humans and most animals, the European Union withdrew it from the market in 2007 (Elenga et al., 2018). This pesticide is a strong cation in liquid formulation, so ingestion, inhalation or application to the skin, eyes, or mucous membranes in concentrated solutions (>20%) can cause serious corrosive injuries. The reaction of this compound with Nicotinamide Adenine Dinucleotide Phosphate form highly reactive free radicals like superoxide anions, which leads to tissue damage by lipid peroxidation. Paraquat is selectively caught and concentrated by lung cells, causing necrosis followed by connective tissue proliferation and pulmonary fibrosis (Albertson et al., 2004).

Paraquat poisoning is dangerous, where most victims, as well as those who have consumed only a tiny portion, will tend to die. The minimum lethal dose is 30 mg/kg, which makes it highly toxic (Elenga et al., 2018; Song et al., 2019). After the intake, pain and swelling in both the mouth and throat, and oral ulcerations, will occur. Nausea, vomiting, and abdominal pain are frequent (Albertson et al., 2004). Its intentional ingestion can cause multiple organ failure, including liver failure and pulmonary fibrosis (Elenga et al., 2018; Song et al., 2019). Although most of adults intoxicated by paraquat die, the mortality rate is lower in children. This difference is due to exposure, which is mostly accidental in children, ingesting lowers doses, as well as the treatments performed and the shorter time elapsed between intake and admission to the emergency room (Qiu & Deng, 2019). There is no

specific antidote for acute paraquat poisoning (Albertson et al., 2004; Qiu & Deng, 2019; Song et al., 2019).

Qiu & Deng (2019) carried out a study in the paediatric department of a university hospital in Western China, from 2012 to 2017, founding 123 paediatric paraquat poisonings. The mean age was 6.8 years, and all lived in rural areas. Approximately 67.5% (83/123) of these patients were accidentally exposed to paraquat, while 32.5% (40/123) ingested this substance intentionally. The age group from 0 to 2.9 years had the highest number of cases (30% of the total). The clinical outcome was discharge for 100 (81.3%) children and death of 2 children (Qiu & Deng, 2019).

22 Chinese children were admitted to Qilu hospital between 2007 and 2012 for oral paraquat poisoning. Most were male (18 *versus* 4 female) and the maximum age corresponded to 14 years. One of the cases was child abuse, another two were accidental and the rest consisted in suicide attempts. The most prevalent symptom was vomiting, followed by chest pressure and abdominal pain (Ge et al., 2014).

Research in French Guiana investigated the number of patients admitted to 3 hospitals for paraquat poisoning from 2008 until 2015. From the 62 patients included, 18 were children under 16 years of age (84% had no psychiatric history). Children ingested less paraquat (48.8 mg/kg) than adults (595.8 mg/kg), which resulted in more deaths among adults (65%) than children (22%) (Elenga et al., 2018).

Organophosphate (OP) and carbamate insecticides have been widely applied for insect control in home and agriculture since the 1960s and can cause poisoning after accidental or intentional exposure (Albertson et al., 2004; Roberts et al., 2012). They’re absorbed by all routes, with faster effects when ingested or inhaled. Dermal exposure can have immediate local effects (local diaphoresis and fasciculations) and late systemic effects (Albertson et al., 2004; King & Aaron, 2015). These two classes have a common mechanism of action, as they inhibit the enzyme acetylcholinesterase (AChE), whose function is to hydrolyse acetylcholine into acetic acid and choline, producing an accumulation of acetylcholine in synapses, neuromuscular junction, and organs, which results in excessive stimulation at these sites. This phenomenon is called cholinergic toxicity. The difference lies in the binding to the enzyme, which is irreversible and reversible by OP's and carbamates, respectively. Thus, this influences treatment approaches for each group and, consequently, acute intoxication by OPs tends to be more severe than that of carbamates as the carbamate-AChE bond naturally hydrolyses and AChE returns to its function within 24 hours to 48 hours (Albertson et al., 2004; King & Aaron, 2015; Roberts et al., 2012).

Acute clinical manifestations reflect the development of the cholinergic crisis and may arise from stimulation of muscarinic, nicotinic and/or CNS receptors. Excess acetylcholine in the 2 receptor subtypes results in different target organ effects (King & Aaron, 2015; Roberts et al., 2012). Therefore, nicotinic symptoms correspond to hypertension, tachycardia, muscle fasciculations, weakness, tremors, and mydriasis; and muscarinic symptoms are miosis, bradycardia, bronchospasm, bronchospasm, salivation and sweating; and a combination of this two may occur (Albertson et al., 2004; King & Aaron, 2015). The CNS can also be affected, indicating severe poisoning, particularly in children (Albertson et al., 2004; King & Aaron, 2015; Roberts et al., 2012). Highlighting that OPs are highly lipophilic, so they are stored in adipose tissue and constant toxicity may happen for some days after exposure. So, redistribution may cause harmful effects again (Albertson et al., 2004; King & Aaron, 2015). Poisonings are particularly common in rural areas and developing countries, where the most powerful pesticides are extensively available (Albertson et al., 2004).

In Egypt, 108 children under 16 years were diagnosed with OPs poisoning during 2019. The number of girls was higher than boys (65 *versus* 43 girls) and the intention was mostly accidental (87%). The mainly route of administration was inhalation (63.8%). Regarding the symptoms, they consisted of miosis and shortness of breath. There were 6 paediatric deaths (Abdel Baseer et al., 2021). Liffhitz et al (1999) detected 36 and 16 cases of paediatric carbamate and OPs poisoning, respectively, at Soroka Medical Center between 1984 and 1996. As in the previous study, most were accidental (46 children). The main symptoms of intoxication were miosis, diarrhoea, hypotonia and stupor (Liffhitz et al., 1999). In 2021, a case of a child ≤ 5 years old in South Africa with OP poisoning was reported. She ingested 6 ml of the pesticide diluted in water, and atropine was administered, and gastric lavage was performed (Sharma & Nin-Gonzalez, 2021). A one-year study (2019) in Egypt observed 108 paediatric cases (≤16 years) of OPs poisoning. 87% of cases were accidents and exposure occurred through several routes simultaneously – inhalation (63.8%), ingestion and dermatological. Bronchorrhea was the most common sign of intoxication. There were 6 fatalities (Abdel Baseer et al., 2021).

Acute cyanide poisoning can cause fast hemodynamic and neurological dysfunction. Possible sources of cyanide exposure include tobacco, mining, agriculture, and hydrogen cyanide gas (HCN) (Parker-Cote et al., 2018). Acetonitrile, a component of some artificial nail removers, is responsible for various paediatric deaths. HCN is produced by combining acid with cyanide salts, corresponding to a conventional by-product of combustion from burning plastics, wool, and many other natural and synthetic products (Albertson et al., 2004). Cyanide salts have a long history of intent for homicide and suicide; ingestion of

approximately 140-250mg is potentially lethal if left untreated. Exposure to HCN even at small amounts can be fatal (Albertson et al., 2004; Parker-Cote et al., 2018). Cyanide absorption can occur by oral, dermal, inhalation and parenteral routes. (Albertson et al., 2004; Parker-Cote et al., 2018).

Parker-Cote et al (2018) performed a systematic review where they identified 102 cases of cyanide poisoning from 1967 through 2015. The most prevalent age group was 20–39 years old (51%), followed by children under 5 years old (44%). It was also observed that 10% of cases occurred between 13 and 19 years old. Clinical findings included respiratory failure (73%), hypotension (54%), arrhythmia (72%), cardiac arrest (20%), seizures (20%) and cyanosis (15%) (Parker-Cote et al., 2018).

Table 4- Studies on pesticides involved in paediatric poisoning

Reference	Study period	Age group	Total intoxication cases	Sex	Cases involving pesticides	Most common toxicants	Other relevant information
Zhang et al (2016)	2012-2016	≥11 years	1349	2713 females (54.2%) 2296 males (45.8)	557 (until 19 years) (11.1%)	Paraquat; Rodenticides; OPs	-
Amiar et al (2017)	2008-2014	All ages	6800	3696 females (4.4%) 2629 males (45.6%)	3137 (48.8%)	Insecticides; Rodenticides	Lethality was higher in new-borns (15.38%), with 68 cases until 19 years old.
Song et al (2019)	2010-2017	<12 years	110	59 females (53.6%) 51 males (46.4%)	110	Paraquat	Boys accounted for 60.5% of the children under 6 years old; all poisoning were accidental. Girls prevail in the group older than 6 years (61.1%) and the causes of poisoning were accidental and suicide.
Elenga et al (2018)	2008-2015	All ages	62	32 females (51.6%) 30 males (48.4%)	18 (29%) (until 16 years)	Paraquat	The duration of hospitalization was bigger in children.
Rizer et al (2018)	1967-2015	All ages	102	29 females (28%) 73 males (72%)	55 (until 19 years) (54%)	Cyanide	Accidental- 18 Homicide- 5 Suicide- 64
Deng et al (2019)	2012-2017	<15 years	123	-	123	Paraquat	-
Brito et al (2015)	2013	≤14 years	45	18 females (40%) 27 males (60%)	12 (26.7%)	Rat poison; Insecticide	All cases were accidental. The age group more prevalent were 1-4 years old.
Oliveira et al (2014)	2008-2013	≤18 years	125	69 females 56 males	15 (12%)	-	Suicide attempt (16.8%) and accidental (23.2%) respectively in adolescents and children. The most prevalent age was 0-4 years old.
Hassan et al (2014)	2011-2012	≤12 years	300	131 females (43.7%) 169 males (56.3%)	86 (28.7%)	OPs; Carbamates: Rodenticides	81% were between 1 and 6 years with 55.5% males and 44.4% females
Lee et al (2018)	2011-2015	≤18 years	590	281 females (47.6%) 309 males (52.3%)	56 (9.5%)	-	≤11 years mainly boys (53.3%) ; ≥11 years mainly girls (53.1%). Children <5 years associated an accidental intoxication. Intentional intoxication with pesticide happens in 2 cases.
Lamireau et al (2022)	1989-1995	≤18 years	2643	Higher rate among boys	98 (3.7%)	-	80% of the patients were ≤4 years and 57% of them were boys; between 12- 15 years female predominance (65%), from all the cases
Pac-Kozuchowska et al (2016)	2008-2012	≤18 years	848	439 females (51,77%) 409 males (48,23%)	33 (3.9%)	-	Pesticide poisoning mostly in rural children and 5 years old.
Truebold et al (2016)	2004-2013	≤19 years	158	54 females (34,2%) 104 males (65,8%)	158	OP's; Carbamates; Rodenticides; Others	127 hospitalizations were accidental, having been more prevalent from 0 to 4 years of age.

Domestic Products

The Toxic Exposure Surveillance System data recorded more than 1,1 million consultations annually in the US about possible poisoning in children <5 years of age in 2012. One-third corresponded to exposure to popular household products such as cosmetics, personal care products, cleaning substances, topical preparations and craft items or office supplies (Schwebel et al., 2015).

A broad variety of individual, family and environmental factors underlie accidental paediatric household poisonings. Thus, family factors are related to the quality and quantity of adult supervision, adequate protection, and storage of household products in the home and adult preparation to respond in case of probable injury. Environmental factors include the number of hazardous substances present in the home and their storage. Individual factors correspond to the child's development and age, as this influences the child's ability to distinguish between safe and dangerous products. So, young children depend on various aspects of objects (colour, texture, among others). Toddlers classify things based mainly on sensory and perceptive information, while pre-schoolers tend to insert different objects in the same group due to their similarities. In addition, the child's ability to recognize and interpret labels and symbols is another potential intoxication factor (Schwebel et al., 2015).

Alcohol is present not only in beverages, but also in various household products, such as mouthwashes and cosmetics. Isopropyl alcohol is widely used as a solvent, antiseptic and disinfectant, being available at home as a 70% solution (Albertson et al., 2004; Rayar & Ratnapalan, 2013). Due to its gastric irritant properties, abdominal pain and vomiting are common and occasionally hematemesis occurs (Albertson et al., 2004).

Cosmetics include perfumes, make-up, and other beauty items, which are commonly ingested by children. Of the cases reported to various poison centers in the US in 2009, there was 1 death attributed to consuming cosmetics. Perfumes and colognes have a greater number of cases and a larger percentage of ethanol (50%-99%), according to Rayar & Ratnapalan (2013). Still, the low incidence of meaningful adverse effects may be a consequence of the lack of palatability of these articles as they can burn and be uncomfortable to ingest (Rayar & Ratnapalan, 2013).

Personal care products were identified primarily as deodorants, shampoos, face and body soaps, shaving items, toothpaste, mouthwash solutions and hand sanitizers. These are easily available to children and are particularly attractive since their conventional use in oral hygiene and can be confused with food-associated fragrances (such as vanilla or fruit). In the 2010 report from various US poison centers, there were over 200000 cases of consumption of personal care products, with no major outcomes or deaths reported. Mouth

solutions contain a significant amount of ethanol – approximately 26.9%, being especially attractive to children due to their high accessibility, charming colours, and sweet taste (Rayar & Ratnapalan, 2013).

Cleaning products are surface polishes, liquids for hands and dishes and detergents and fabric softeners. These are stored in common places and can be scented and have attractive colours. In USA, the total for the cleaning products category was nearly 125,000 paediatric ingestions during 2010 (Rayar & Ratnapalan, 2013). Detergents are synthetic surfactants chemically categorized as anionic, non-ionic, or cationic. Most products also have bleaching, bacteriostatic or enzymatic agents. Accidental consumption of detergents by kids is very common, but serious toxicity hardly happens (Albertson et al., 2004). These can precipitate and denature proteins, are tissue irritants, and have keratolytic and corrosive activities. Cationic detergents are the most dangerous as they can have corrosive effects if ingested (Albertson et al., 2004; Rayar & Ratnapalan, 2013). Instant impulsive vomiting follows oral ingestion; in high doses they can cause diarrhoea and hematemesis (Albertson et al., 2004). Disinfectants are believed to cause minimal risk, but in higher quantities, they can provoke corrosive effects, acidosis, CNS depression and liver and kidney damage. One of the most affordable and visible forms of disinfectants, alcohol-based hand sanitizers, pose a substantial risk of intoxication due to their 60% to 95% ethanol content. A case of a 3-year-old child suspected of having ingested almost 45 ml of hand sanitizer, presented with hypothermia and stupor in 2010 (Rayar & Ratnapalan, 2013).

This range of products commonly found in the home are, for the most part, completely non-toxic or have tiny or no toxicity after normal unintentional exposures. Though, the taste or texture of the item may be unpleasant or produce mild stomach discomfort. In addition, some of the products may create a foreign body effect or choking hazard, differing on the design and the age of the kid. Stomach cramps, vomiting, or diarrhoea may occur, but are usually mild and self-limiting (Albertson et al., 2004).

Table 5- Studies on domestic products involved in paediatric poisoning

Reference	Study period	Age group	Total intoxication cases	Sex	Cases involving domestic products	Other relevant information
Berta et al (2020)	2012-2017	≤14 years	1030	463 females (45%) 567 males (55%)	bleach products: 96 surface cleaners: 55 dish washing liquids: 37 drain cleaners: 18 nail polish remover: 16 (54 cases of cosmetic products intoxication).	Accidental- 882 Therapeutic error- 109 Suicide attempt- 24 Recreational purpose- 15
Brito et al (2015)	2013	≤14 years	45	18 females (40%) 27 males (60%)	detergent, bleach, stain remover: 11 (24.4%)	All cases were accidental. The age group more prevalent were 1-4 years old.
Gokalp, Gamze (2019)	2017	≤18 years	453	202 females (46.4%) 233 males (53.6%)	detergents: 211 (46.6%) cosmetics: 11 (2.4%)	From all the cases, accidental poisoning in males (233 vs 165) and suicide attempt mainly occurs in females (37 vs 10) and
Oliveira et al (2014)	2008-2013	≤18 years	125	69 females 56 males	5 (4%)	Suicide attempt (16.8%) and accidental (23.2%) respectively in adolescents and children. From all cases, the most prevalent age was 0-4 years old.
Hassan et al (2014)	2011-2012	≤12 years	300	131 females (43.7%) 169 males (56.3%)	bleach, disinfectant, laundry products: 51 (17%)	81% were between 1 and 6 years with 55.5% males and 44.4% females from all the cases
Hoikka et al (2013)	1991-2010	≤6 years	334	143 females (40.1%) 191 males (59.9%)	dishwasher powder: 31 (9.3%) ethylene glycol: 17 (3.9%)	The incidence of all poisonings was higher in boys
Lee et al (2018)	2011-2015	≤18 years	590	281 females (47.6%) 309 males (52.3%)	cleaning substances: 45 (7.6%) personal care products: 21 (3.6%) deodorizers: 5 (0.8%)	≤11 years mainly boys (53.3%) ; ≥11 years mainly girls (53.1%). Children <5 years associated an accidental intoxication.
Lamireau et al (2022)	1989-1995	≤18 years	2643	Higher rate among boys	cleaning products: 618 (23.8%) cosmetics: 77 (3%) household items: 36 (1.4%)	80% of the patients were ≤4 years and 57% of them were boys. Between 12- 15 years female predominance (65%), from all the cases.
Pac-Kozuchowska et al (2016)	2008-2012	≤18 years	848	439 females (51.77%) 409 males (48.23%)	67 (7.9%)	Domestic products poisoning mostly in rural children and under 5 years old.
Mintegi et al (2006)	2001-2002	≤19 years	2157	1078 females (50%) 1078 males (50%)	624 (28.9%)	Children ≤ 6 years represented the most prevalent group (567). Sodium hypochlorite was the main product involved.
Fook et al (2013)	2007-2010	All ages	7354 (653 household products)	362 females (55.4%) 291 males (44.6%)	305 cases (46.8%) (132 males and 173 females until 19 years)	Most of the cases occur in children ≤9 years (196). Boys were more prevalent in this group.

Carbon Monoxide

Carbon monoxide (CO) is a significant cause of poisoning worldwide. In the US, approximately 50,000 emergency room visits each year are assigned to the CO according to a study carried out in several states of USA during 2007 (Cho et al., 2008). Sources of CO include internal combustion engines, fires, and gas-powered appliances such as ovens and stoves. This is a colourless, odourless, non-irritating gas, designated a “silent killer” as exposure may not be detected until the onset of severe symptoms (Albertson et al., 2004; Calabuig, 2004; Christensen et al., 2019; Karapirli et al., 2013). CO is produced by the incomplete combustion of organic substances and is present in the blood at a concentration of less than 5% (Albertson et al., 2004; Calabuig, 2004; Karapirli et al., 2013). Poisonousness is a result of cellular hypoxia. CO attaches to haemoglobin with an affinity 250 times greater than that of oxygen, causing a decreased oxyhaemoglobin saturation and reduced oxygen-carrying ability in the blood, thereby impairing the supply of oxygen to tissues. It can bind to myoglobin, contributing to diminished myocardial contractility. The carboxyhaemoglobin complex progressively detaches upon removal from exposure, where its approximate elimination during high-level oxygen treatment is 74 minutes (range 24 to 148 minutes) (Albertson et al., 2004; Cho et al., 2008; Christensen et al., 2019). In children exposed to CO, initial acute neurological symptoms such as varying degrees of disturbance of consciousness and seizures may occur. In addition, they may present with a range of nonspecific signs, like vomiting, headache, or dyspnoea, and other symptoms; dizziness, weakness, difficulty concentrating or confusion, visual changes, chest pain and muscle cramps, some common to adults (Albertson et al., 2004; Cho et al., 2008).

Cho et al (2008) observed 30 cases of children poisoned by CO between 1996 and 2007 in Taiwan, with a predominance of females (19 *versus* 11 males). The mean baseline carboxyhaemoglobin level was 35.3 ± 13.9% (range: 7.4 - 60.3%). There was only 1 death of a 9-year-old girl (Cho et al., 2008). Karapirli et al (2013) carried out a systematic review in the paediatric population where they obtained 20 fatal cases due to CO from 1984 until 2011 in Turkey. The highest prevalence was in the group aged 2 to 12 years (55%), followed by children aged 1 day to 2 years (25%) (Karapirli et al., 2013).

1.2 Route of Intoxication

The magnitude of damage produced by toxic elements differs according to the exposure means. Oral ingestion corresponds to the main route of administration of toxics (Gokalp, 2019). Vilaça et al (2020) observed ingestion (82.7%) as the most frequent route and dermal absorption (5.1%) the less (Vilaça et al., 2020). Lee et al (2019) also reported the oral route as the main one in 463 cases (78.5%); this was followed by inhalation (19.2%; n=113), stinging (2%; n=12) and contact (0.2%; n=2) (Lee et al., 2019). The same result was demonstrated by Koh et al (2018); Hassan et al (2014) and Berta et al (2020) (Berta et al., 2020; Hassan & Siam, 2014; Koh et al., 2018).

1.3 Intent of intoxication

During puberty, fast physical, mental and emotional changes occur. So, this age group becomes susceptible to risky behaviours like voluntary intoxications (Albertson et al., 2004; Berta et al., 2020; Lamireau et al., 2022; Nistor et al., 2017; Pac-Kozuchowska et al., 2016). This is defined, according to the World Health Organization (WHO), as a non-fatal action in which a person deliberately ingests a substance in overdose (Nistor et al., 2017). This type of intoxication is used as a method of self-inflicted injuries and suicide attempts among teenagers, indicating a community health issue in industrialized countries (Nistor et al., 2017).

According to the 2012 report of the American Society of Toxicology Center, adolescents can be distributed into 3 groups of intentional ingestion: voluntary abuse, intentional misuse, and suicide attempted (Nistor et al., 2017). The term suicide involves suicidal feelings, strategies, and acts, as well as attempted and achieved suicide. Thus, the suicide attempt is any performance initiated by the self with the objective of leading to death, such as the ingestion of certain compounds/large amounts of substances. In addition, self-mutilation may also occur. According to Becker & Correll (2020), 7% of adolescents who experience therapy after a suicide attempt, no matter the seriousness, try to kill themselves again (Becker & Correll, 2020). It should be noted that during this age group, voluntary intoxication can be not only an episode of suicide attempt, but also a call for help or a demonstration, so an act of this gravity shouldn’t be ignored (Nistor et al., 2017).

Therefore, it is essential to detect risk factors and predictors to guarantee adequate preventive care (Nistor et al., 2017). One of the primary risk factors for self-intoxication is the female gender, because girls consider suicide more often. (Berta et al., 2020; Lamireau et al., 2022; Nistor et al., 2017; Pac-Kozuchowska et al., 2016). In addition, the use of medications as a toxic agent is also more common in females.

In general, the main harmful toxic implicated in deliberate intoxication are medicines. Thus, the literature indicates that females have a higher risk for conventional suicidal ideation/depression methods, while risk actions (like alcoholism or drug abuse) are more frequent in boys (Nistor et al., 2017). Another risk factor corresponds to substance abuse, which appears to be independent for self-inflicted injuries and suicidal behaviour. The social factor is also important in poisoning during puberty, both in family and school environments: conflicts in both environments; an authoritarian parenting style; a neglectful-rejecting style related with absence of love (inflexible families); absenteeism; parental separation cases; struggles with the sexual/affective partner; sexual, physical or mental abuse; conflict with sexual orientation; a sudden or severe loss; migration; dysfunctional families; school flop; desire for integration; among others (Albertson et al., 2004; Nistor et al., 2017; F. F. S. Oliveira & Suchara, 2014). The inherent psychiatric disease presents a significant risk of practicing self-harm and may stimulate to a suicidal action and relapse. In these we can include depression, which is quite present in females (Albertson et al., 2004; Nistor et al., 2017; F. F. S. Oliveira & Suchara, 2014). Some risks may arise from prescribing antidepressants such as selective serotonin reuptake inhibitors, which are indicated as responsible for behavioural triggering in teenagers with suicidal thoughts (Becker & Correll, 2020). Thus, we can say that there is no single cause of self-intoxication, since the various events generate negative emotions and can lead to thoughtless behaviours (Berta et al., 2020; Lamireau et al., 2022; Pac-Kozuchowska et al., 2016).

For younger children, suicide attempts and completed suicide are very rare as they don’t have the necessary cognitive maturity (Becker & Correll, 2020). Therefore, the probability of intentional application by an older child or adult should be accepted, as these are more prone to abuse or neglect (Albertson et al., 2004). Dayasiri et al (2020), in Sri Lanka over a seven-year period (2007-2014), observed that in 13% of children, the dose was wrongly administered by an adult (Dayasiri et al., 2020).

Accidental intoxication is a worldwide health problem amongst children and teenagers, with approximately 45,000 deaths per year and an incidence of 1.8 per 100,000 inhabitants, according to WHO (WHO, 2008). In addition, it generates a significant number of hospitalizations (Vilaça et al., 2020). These are typically seen in infants, reducing over the course of the child's emotional and cognitive growth (Oliveira & Suchara, 2014). In general, there are several factors that contribute to a child's intoxication, such as the type of toxic, youth development, parental supervision and security methods imposed in the home. According to Schmertmann et al (2013), behavioural factors such as the child's conduct (age, sex, developmental status and personality); caregiver supervision (age, parental stress, personality, physical and mental well-being and sociodemographic

condition - marital status, scholar level and profession); the caregiver-child relationship and the environment (size and type of housing, categories of substances present and the child's access to products) are both risk and protective factors for the child related to accidental poisoning (Schmertmann et al., 2013).

The impulsive and curious behaviour (acquiring mobility; strong oral orientation - trying to put everything in their mouths; tendency to explore the environment; interest for new and colourful things) typical of young children raise the risk of poisoning accidents (Abbas et al., 2012; Ahmed et al., 2015; Albertson et al., 2004; Berta et al., 2020; Brito & Martins, 2015; Hassan & Siam, 2014; Hoikka et al., 2013; Koh et al., 2018; F. F. S. Oliveira & Suchara, 2014; Pac-Kozuchowska et al., 2016; Schmertmann et al., 2013). Yet, the supervisory choices (like the lack of knowledge, mainly about the toxicity of agents, inattention to risks and insufficient supervision) and safety practices can be affected by caregivers' perceptions of the child's evolving level. Therefore, an inaccurate perception can end in insufficient supervision and lack of storage practices, leading to the risk of child exposure (Abbas et al., 2012; Dayasiri et al., 2020; Schmertmann et al., 2013). Children, especially pre-schoolers, remain most of their time at home, where the risk of exposure is associated with access to various types of substances because products aren’t stored or used correctly. So, accidental poisoning in residential home is quite common in the child and youth population (Brito & Martins, 2015; Dayasiri et al., 2020; Hassan & Siam, 2014; Santos et al., 2021; Vilaça et al., 2020).

Household products, cosmetics, hygiene products and pharmaceutical agents are the toxic substances most utilized by kids (Berta et al., 2020; Brito & Martins, 2015; Hoikka et al., 2013; Vilaça et al., 2020). In terms of medicines, both in Europe and the US, there is a prevalence of paracetamol, psychotropics (antipsychotics, anxiolytics, among others), analgesics, antihistamines, and cough/flu preparations (Albertson et al., 2004; Berta et al., 2020; Hoikka et al., 2013; Koh et al., 2018). All these products are generally ingested because they are colourful, attractively packed, and easily available in the home (Koh et al., 2018). Agarwal et al (2020), observed, during an 8-month study period (2017) in USA, that among exposures to prescription drugs, 81.1% involved drugs intended for adults and that grandparent drugs were involved in four times as many exposures because they had been shifted to alternative recipients, such as pill holders and plastic sandwich bags (Agarwal et al., 2020). The most common spaces where children obtain medication involve bags or backpacks and bedside tables (Albertson et al., 2004). Chemicals used in household activities (detergents, washing powder, bleach, and plungers) can be found in most homes in liquid form, often stored improperly and their colourful appearance is attractive to children.

In addition, these products are often sold in bottles without identification labels to inform about their use (Santos et al., 2021; Vilaça et al., 2020).

Overall, about 60 to 70% of childhood patients with poisoning who are admitted to the emergency room in Oulu hospital (1991-2010) were asymptomatic (Hoikka et al., 2013).

1.4 Gender and age susceptibility

According to previous studies, the age distribution of paediatric intoxication seems to have two peaks, with the majority occurring in children between 1 and 5 years (toddlers and pre-schoolers) and again in adolescents (over 14 years) (Abbas et al., 2012; Ahmed et al., 2015; Albertson et al., 2004; Berta et al., 2020; Hassan & Siam, 2014; Hoikka et al., 2013; Koh et al., 2018; F. F. S. Oliveira & Suchara, 2014; Pac-Kozuchowska et al., 2016; Schmertmann et al., 2013). In 2010, the New South Wales Poisons Information Center received over 23,500 phone calls related to accidental poisoning in children ≤ 4 years (Schmertmann et al., 2013).

Associating age with gender, was also noted that male children are more subjected to unintentional poisoning at earlier ages and that the greatest rate of deliberate poisoning occurs in females during adolescence (Azab et al., 2016; Gokalp, 2019; Hassan & Siam, 2014). This higher rate of intention in females is explained by the greater propensity of women to incorporate emotional and behavioural problems. Furthermore, the fact that, as mentioned before, in suicide attempts, women tend to utilize non-violent methods, such as asphyxiation from CO intoxication, drug ingestion and alcohol intoxication; in contrast, men tend to use more violent modes, such as firearms or high jumps (Azab et al., 2016; Becker & Correll, 2020).

To reinforce this knowledge, numerous epidemiological studies on unintentional poisoning in children show a steady pattern in relation to age and sex, being predominant in children ≤ 6 years and males. (Abbas et al., 2012; Ahmed et al., 2015; Berta et al., 2020; Brito & Martins, 2015; Hassan & Siam, 2014; Lamireau et al., 2022; Pac-Kozuchowska et al., 2016). This difference in this type of intoxication relates to behavioural factors, because boys are known to be more active and restless, and by social and cultural factors, since more surveillance is given to girls, while boys are freer in their play and, therefore, are more exposed to the risks of the home environment (Ahmed et al., 2015; Albertson et al., 2004; Greene et al., 2005; Pac-Kozuchowska et al., 2016).

1.5 Intoxications in urban versus rural environments

The extent of paediatric poisonings differs from country to country (Ahmed et al., 2015). This diversification across countries and populations has been associated to socioeconomic status and cultural customs plus regional industrial and agricultural practices. Exposure incidence reflets product disposal, child availability and packaging design (Azab et al., 2016). The clinical outcome depends on factors such as the type of poisonous agent and the ease of access to medical facilities, which are directly connected to the home location (Vilaça et al., 2020).

In high/middle income level countries, paediatric poisoning is the fourth leading cause of accidental injuries, after fires, road accidents and drowning. In these, items more available to kids, like cosmetics and personal care products, cleaning products, analgesics and cough and flu pharmaceuticals are accountable for most of these exposures. In developing countries (Africa and low-income level countries in Europe and in the Western Pacific regions), kerosene, paraffin and pesticides are the products that cause greater cases of accidental poisoning in children. The intoxication rates are about four times greater than in high income level countries, according to the WHO report. This is because of poor regulation of drugs and chemicals, lack of surveillance systems, scarcity of medical services and easy access. In addition, the available products have higher toxicity. Pesticides, for example, are widely used in agriculture, but also in the domestic environment, making them the most prevalent toxic agent in these types of countries (Ahmed et al., 2015; Azab et al., 2016). All these facts contribute to the highest mortality rates (Alinejad et al., 2017). In the 2000s there were more than three million cases of poisoning in young adults, with 90% of these deaths occurring in developing countries (Ahmadi et al., 2010). According to WHO, in 2012, the mortality rate from poisoning was 0.5 per 100,000 and 2 per 10,000 population in developed and developing countries, respectively (Gokalp, 2019).

In general, urban children prevail in hospitalization for acute intoxication. This could be a consequence of more frequent direct access to the health services closest to the housing or – fewer possible – a genuinely smaller prevalence of intoxication among rural kids (Pac-Kozuchowska et al., 2016). Vilaça et al (2020) observed, in 2013, that a high proportion of child victims resided in urban areas in Brazil – 94.9% of cases (Vilaça et al., 2020). Lamireau et al (2022) reported a lower incidence of poisoning in children living in the surrounding countryside (0.6/1000) than in those living in the city of Bordeaux (2.2/1,000) or its suburbs (1.9/1,000) from 1988 until 1995 (Lamireau et al., 2022). Pac-Kozuchowska et al (2016) also found that many paediatric patients were from urban areas (64.5%), while a third were from Poland rural areas (35.5%). The study (2008-2012) also revealed a

meaningful correlation between gender and the nature of intoxication in urban children. Among urban girls, intentional intoxication was more frequent (58%), although among boys' accidental intoxication was more common (65.6%). Between rural children, unintentional poisoning was equivalent- boys (68%) and girls (54%) (Pac-Kozuchowska et al., 2016).

1.6 General management of poisoning

In the past, intoxication was believed as one clinical entity that might be cured in the same manner for all toxics: "detoxifying methods" and alleged collective antidotes, thought to be capable of neutralizing the effects of all poisons. Nowadays, new analytical toxicology and quick ease of access to intoxication information centers allow cases to be treat with individuality, with a much more precise risk evaluation. The specific treatment depends on the toxic compound and the dose implicated. It should be noted that patients who don't show signs or only mild symptoms of intoxication, the situation can become dangerous, since there are substances that have, for example, a long latency period, such as paracetamol (Müller & Desel, 2013). According to Calabuig (2004), maintenance and treatment of acute intoxication can be divided into 4 groups: maintenance of vital functions, mainly cardiorespiratory, with application, if necessary, of cardiac massage, orotracheal intubation and assisted ventilation; limit the absorption of the toxic as much as possible; neutralize the substance in order to block its effect and eliminate the compound to reduce its concentration in the body (Calabuig, 2004).

Administration of activated charcoal is a less invasive technique of reducing absorption and less unsafe when used for the correct indications. Thus, it should not be administered before understanding the adsorptive characteristic of the consumed compound. It is contraindicated after intake of corrosive substances (such as inorganic acids), surfactants, or liquid hydrocarbons, and every time that respiratory tract is occupied (with intubation). The major danger linked with the administration of activated charcoal is aspiration. This substance can be use in paediatric intoxications (Hoikka et al., 2013; Müller & Desel, 2013).

Gastric lavage is associated with serious problems such as aspiration, hypoxia, pneumonia, perforation, and laryngospasm, so its indication for decreasing the absorption of compounds is limited. This procedure must only be counted in life-threatening cases within 60 minutes of consumption.

Urine alkalinization is performed by intravenous administration of sodium bicarbonate (pH over 7.5), being suggested mostly for patients with salicylate poisoning. Treatment is aimed at increasing drug elimination and thus preventing acidosis (Müller & Desel, 2013).

Haemodialysis is an appropriate technique for the fast excretion of short-chain alcohols like methanol and ethylene glycol, especially once poisoning has already produced acidosis. It is also used for other substances, including salicylates, valproate, lithium, carbamazepine, phenytoin, and metformin (Müller & Desel, 2013).

The administration of an efficient antidote is thought the best therapy for an intoxication. Acetylcysteine for paracetamol poisoning and dimethicone for surfactant ingestion and fomepizole for methanol or glycols, as an example (Müller & Desel, 2013).

1.7 Prevention and child safety at home

To avoid accidental poisoning, some measures must be implemented in the domestic environment, as well as increased caution/supervision by the child's legal guardians. In relation to the home, the storage of medicines and cleaning products should be done in places inaccessible to children, not being visible. Also, mustn't store chemicals in food containers or place them in the same cupboards as food. On the part of the family, attention must be paid to the risks of the different products (which are usually listed on the packaging); administer the appropriate dose of paediatric drug; not use illegal products; not change the original packaging of substances; not administering medicines in front of children and giving preference to packaging of cleaning and pharmaceutical products that have safety lids (Albertson et al., 2004; Brito & Martins, 2015; Santos et al., 2021). It is also important, when intoxication occurs, that professionals provide education on its prevention. Evidence suggests that, at present, the emergency team only provides advice to parents on preventing poisoning in a minority of cases (Ahmed et al., 2015; Greene et al., 2005; Pac-Kozuchowska et al., 2016).

2. Aims

Although children's deaths from poisoning have been decreasing, this remains a serious concern. In order to establish the dimension and characteristics of the problem, as well as to increase the specificity of preventive strategies, it is important to conduct epidemiological assessments in different countries and regions.

In Portugal, the epidemiology of poisoning in the paediatric population has not yet been sufficiently studied. So, it is imperative to obtain data on the profile of childhood intoxications in specific locations to allow an exhaustive characterization of these and further assist the competent authorities in the identification of priority areas of intervention. This dissertation aims to retrospectively analyse the epidemiology of poisoning in children (from 0 to 18 years old) admitted to the Paediatric Emergency Unit of the *Centro Hospitalar de São João*, EPE (CHSJ), Porto (Portugal) from 2010 to 2018.

3. Material and Methods

Study Population

This study will focus on all patients ≤ 18 years that were admitted to the Paediatric Emergency Unit of the CHSJ, as well as those transferred from other hospitals, due to intoxication. The study period consists of 1 January 2008 until 31 December 2018. Exclusion criteria correspond to intoxication due to I) food poisoning; II) animal bites and stings; III) incorrect diagnosis of poisoning through the International Classification of Diseases 9 (ICD-9); and IV) duplicate cases. All clinical reports included were available from the CHSJ database.

Ethical concerns

To carry out this study, it was necessary to request the prior approval of the Ethics and Health Committee of the CHSJ as it involved the processing of personal health data that had been collected previously (secondary use). In addition, authorization to access the clinical files was also solicited to the competent authority for the re-use of clinical data (*Responsável pelo Acesso à Informação*, RAI).

Study Design

Data were obtained from the hospital reports of patients admitted to the Paediatric Emergency Unit of the CHSJ whose diagnosis was "Intoxication". Information regarding intoxication (including time and type of intoxication, intention, toxic agent, time elapsed between exposure and hospitalization, clinical symptoms and signs, treatment, clinical evolution, discharge destination) and the characteristics of the child (including age, sex, school cycle, postal code of residence, place of origin in the case of patients referred from other hospitals) were collected. Children were classified into four age groups: i) 0-2 (new-borns, babies, and toddlers); ii) 3–5 (pre-schoolers); iii) 6–12 (school children) and iv) 13–18 (teenagers). The classes of drugs used as toxic agents were categorized according to the *Prontuário Terapêutico*.

Statistical analysis

All data were statistically analysed using the IBM Statistical Package for the Social Sciences (SPSS) Statistics 27® software. The chi-square test was used to access statistical significance between categorical variables, while the Chocran test was applied for multiple groups in the same variable. A $p<0.05$ was considered to assume statistically significance.

4. Results

During the study period (8 years), from the 1st of January 2010 to 31st of December 2018, 1,694 cases of paediatric intoxication were admitted to the CHSJ emergency unit. However, some of these were excluded from the study, according to the criteria proposed above: 98 coincident cases in both databases provided by the CHSJ (i.e., informatic database, which was created from 2014 on; and the medical paper files, before that date); 9 cases of food poisoning; 1 case of medical reassessment; 1 case of intoxication by fungi; and 1 case due to lack of information. Thus, a total of 1,584 cases of paediatric poisoning was analysed.

Sample characteristics

Of all the cases (Table 6), females prevailed over males with 822 (51.9%) and 762 (48.1%) cases, respectively, but this difference was not statistically significant ($p<0.5$). The age group with the highest number of poisonings corresponded to adolescents 1,013 cases (64.0%), followed by toddlers (300 cases; 18.9%), pre-schoolers (169 cases; 10.7%) and school children (102 cases; 6.4%). In adolescents, it was possible to verify a predominance of females in relation to males, with the opposite being found in younger age groups (from birth to 5 years old) ($p<0.001$). Most children lived in the municipality of Porto (901 cases; 56.9%).

Table 6- Characteristics of the paediatric population

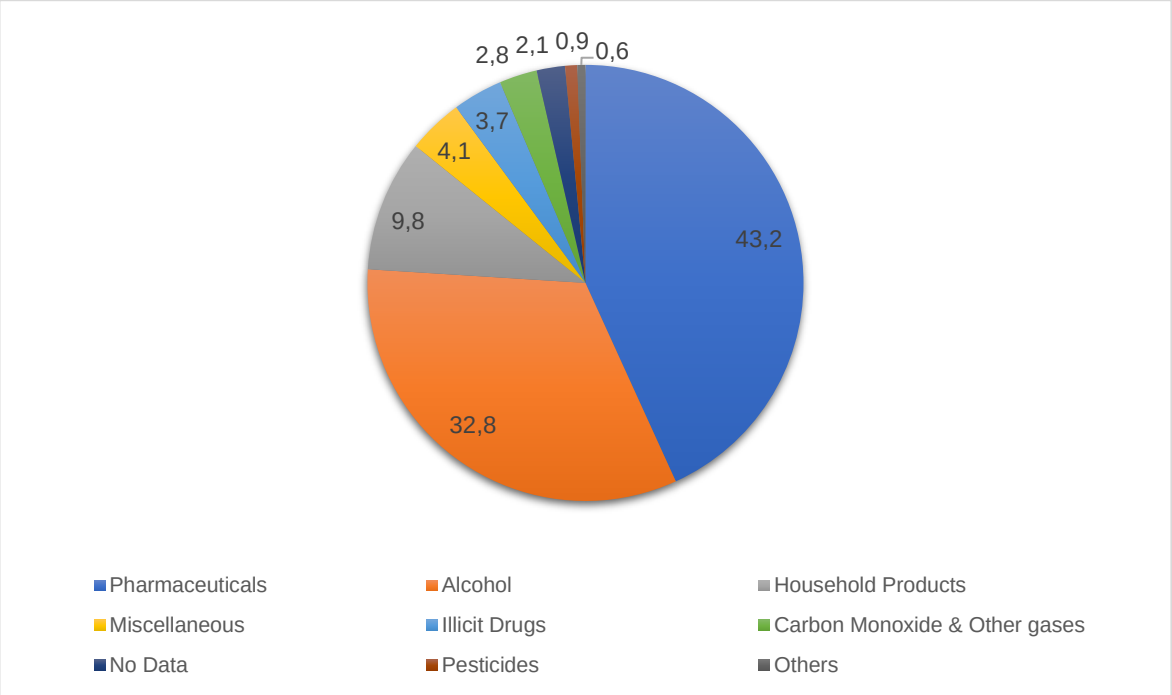
		Age groups (years)				**Total**
		≤2	3-5	6-12	13-18	
		300 (18.9%)	169 (10.7%)	102 (6.4%)	1,013 (64.0%)	1,584 (100%)
		N (%)	N (%)	N (%)	N (%)	N (%)
Gender	Male	160 (53.3)	102 (60.4)	54 (52.9)	446 (44.0)	762 (48.1)
	Female	140 (46.7)	67 (39.6)	48 (47.1)	567 (56.0)	822 (51.9)
Residence	Porto	169 (56.3)	100 (59.2)	42 (41.2)	590 (58.2)	901 (56.9)
	Gondomar	31 (10.3)	22 (13.0)	9 (8.8)	89 (8.8)	151 (9.5)
	Matosinhos	26 (8.7)	10 (5.9)	11 (10.8)	87 (8.6)	134 (8.5)
	Valongo	25 (8.3)	11 (6.5)	10 (9.8)	66 (6.5)	112 (7.1)
	Maia	18 (6.0)	15 (8.9)	16 (15.7)	60 (5.9)	109 (6.9)
	Outros	28 (9.3)	11 (6.5)	14 (13.7)	113 (11.2)	166 (10.5)
	No data	3 (1.0)	0 (0.0)	0 (0.0)	8 (0.8)	11 (0.7)

Intoxication characteristics

The type of intoxication (Figure 1) was divided into 9 groups: I) pharmaceuticals (which includes all medicines subjected and not subjected to medical prescription); II) alcohol; III) illicit drugs (amphetamines, cannabis, hallucinogenic drugs,

NPS, sympathomimetic drugs and opioids); IV) carbon monoxide & other gases; V) pesticides (fertilizers, herbicides, insecticides, organochlorine compounds, organophosphate compounds, repellents and rodenticides); VI) household products (office supplies, disinfectants, detergents, cosmetics and cleaning products); miscellaneous (various toxics of the previous classes were involved); and others (fire extinguisher dry powder and oil derivatives).

Figure 1 – Type of paediatric intoxication

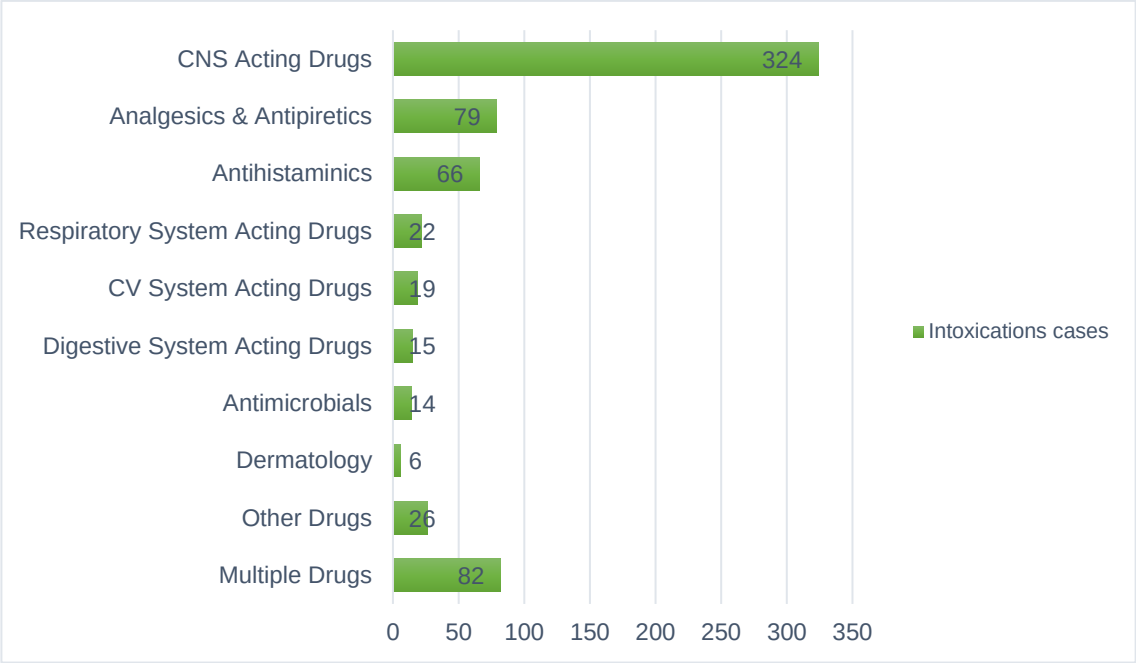


Pharmaceuticals were the most common type of agent ($p<0.001$, compared to other groups) involved in poisoning in our study (685 cases; 43.2%), followed by alcohol (519 cases; 32.8%) and household products (155 cases; 9.8%). However, in 34 cases (2.1%) it was not possible to determine the toxic agent involved. As expected, cannabis was the most frequent illegal drug (33 cases; 55.9%). Soon after, the NPS with 14 cases (23.7%). There were 4 cases (6.8%) where several illicit drugs were used simultaneously. In household products, cleaning products and disinfectants were the most prominent groups, with 65 (41.9%) and 41 (25.2%) cases, respectively. The pesticides displaying the highest number of poisonings consisted of rodenticides (5 cases; 35.7%). Consumption of alcohol together with illicit drugs represented the majority of intoxication cases (46 cases; 70.8%) in the miscellaneous group.

As we can see in Figure 2, the pharmaceuticals with the greatest number of paediatric cases corresponded to the class of drugs that act on the CNS (47.3%; $p<0.001$, compared to all other classes), followed by analgesics and antipyretics (11.5%; $p<0.5$),

antihistaminics (9.6%; p<0.5), products with action on the respiratory system (3.2%; p<0.5), and other drugs (3.8%; p<0.5). In other drugs are included medicines that act at the hormonal level, supplements, homeopathies, antidiabetics, vitamins and minerals, and drugs that act on the genitourinary system. There were 82 cases (12%) of intoxication by pharmaceuticals of different classes.

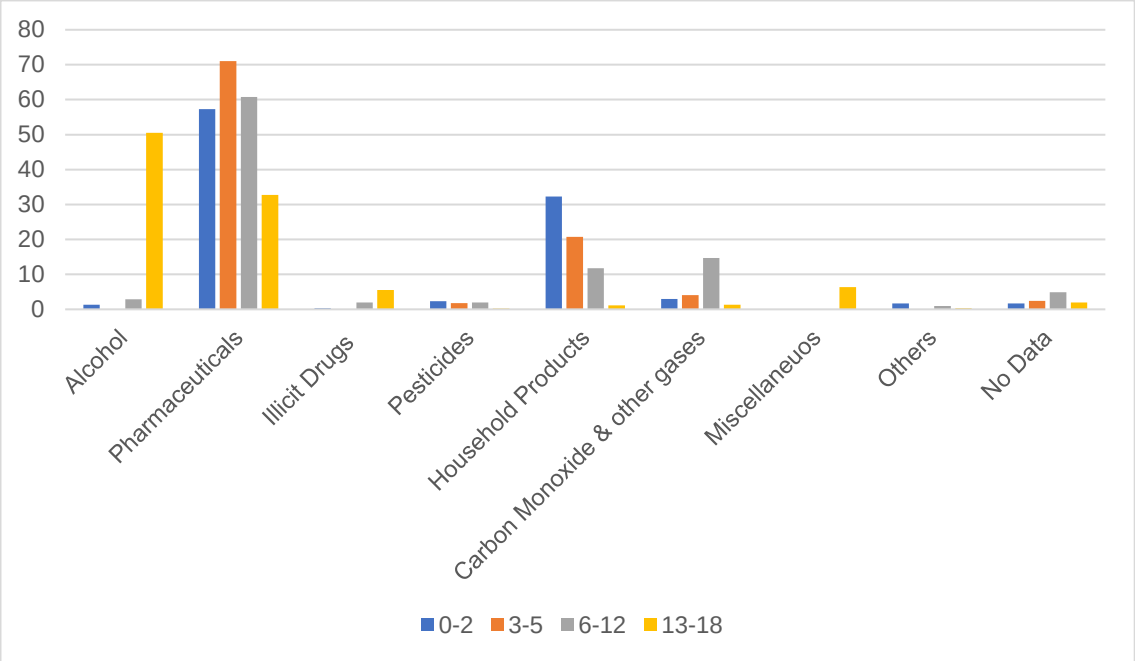
Figure 2- Intoxications by each class of pharmaceuticals



CNS, Central Nervous System. CV, Cardiovascular System. Other drugs: medicines that act at the hormonal level, supplements, homeopathies, antidiabetics, vitamins and minerals, and drugs that act on the genitourinary system.

In our study (Figure 3), it was found that younger children (toddlers and pre-schoolers) were mainly admitted to the hospital due to pharmaceuticals (292 cases; 62.3%), followed by household products (132 cases; 28.1%) (p<0.001, compared with all other toxics). While, in the group of adolescents, alcohol was the main intoxication agent (512 cases; 50.5%). Pharmaceuticals also prevailed in this age group with 331 cases (32.7%). These two intoxication agents had a significant difference (p<0.001), compared with all other groups.

Figure 3- Intoxication cases by type of poisoning *versus* age



Pharmaceutical poisoning (441 cases; 53.6%) ($p<0.001$, compared with all other groups) represented the highest number of admissions to the emergency room, among females (n=822). In this sex group, pharmaceuticals were the major toxic used by adolescents (275 cases; 62.4%) compared to younger children (86 cases (19.5%) in the group of children aged ≤2 years and 55 (12.5%) from 3 to 5 years old; $p<0.015$). Next was alcohol and illegal drugs with 220 (98.2%) and 21 (87.5%) adolescent girls intoxicated, respectively ($p<0,001$, compared to other ages groups). Our data also emphasize that intoxication with agents from the miscellaneous class occurred exclusively in teenagers.

In children aged ≤2 years, in addition to the prevalence of pharmaceuticals (86 cases; 61.4%), household products also displays a high number of intoxications (43 cases; 30.7%).

It was also possible to identify 220 cases (26.8%) of intoxication by drugs acting on the CNS (compared to 104 cases in males; $p<0.001$) and 64 admissions (7.8%) for multiple medicine classes in females (while in boys it was only observed 18 cases; 2.4%; $p<0.001$). The most common psychoactive were anxiolytics, sedatives and hypnotics (123 cases; 55.9%), antidepressants (34 cases; 15.5%) and antipsychotics (22 cases; 10%). Figure 4 and Table 7 shows the distribution of intoxications by the type of poisoning *versus* of age, in girls.

Figure 4- Intoxication cases by type of poisoning versus age, in females

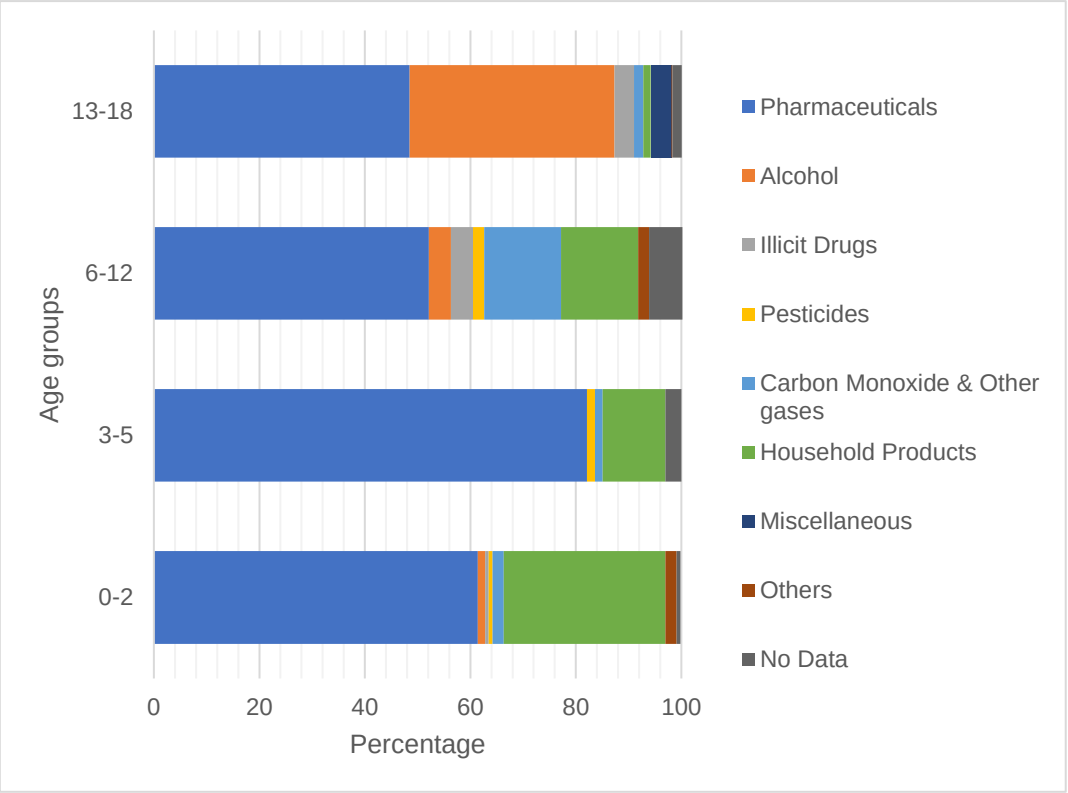


Table 7- Intoxication cases by type of poisoning versus age, in female

	Age groups (years)			
	≤2	3-5	6-12	13-18
	N (%)	N (%)	N (%)	N (%)
Pharmaceuticals	86 (61.4%)	55 (82.1%)	25 (52.1%)	275 (48.5%)
Alcohol	2 (1.4%)	0 (0.0%)	2 (4.2%)	220 (38.8%)
Illicit Drugs	1 (0.7%)	0 (0.0%)	2 (4.2%)	21 (3.7%)
Pesticides	1 (0.7%)	1 (1.5%)	1 (2.1%)	0 (0.0%)
Carbon Monoxide & Other gases	3 (2.1%)	1 (1.5%)	7 (14.6%)	10 (1.8%)
Household Products	43 (30.7%)	8 (11.9%)	7 (14.6%)	8 (1.4%)
Miscellaneuos	0 (0.0%)	0 (0.0%)	0 (0.0%)	22 (3.9%)
Others	3 (2.1%)	0 (0.0%)	1 (2.1%)	1 (0.2%)
No Data	1 (0.7%)	2 (3.0%)	3 (6.3%)	10 (1.8%)

Alcohol intoxication (295 cases; 38.7%) ($p<0.001$, compared with all other groups) consisted of the greatest number of cases in males (n=762). Adolescent boys were the ones who most consumed alcohol (292 cases; 65.5%), compared to other age groups ($p<0.001$). Here we can also emphasize the use of illicit drugs (35 cases; 7.8%) and miscellaneous drugs (43 cases; 9.6%) as characteristic of this age group. At younger ages, namely in toddlers and pre-schoolers, pharmaceuticals prevailed with 86 (53.8%) and 65 admissions (63.7%) to the emergency room ($p<0,015$, in contrast to other age groups). Next, in the same age groups, household products appear in 54 (33.8%) toddler and 27 (26.5%) pre-

schooler cases. Males predominated both in the utilization of illegal drugs simultaneously with alcohol (36 cases; 4.7%) and pesticides (11 cases; 1.4%). Figure 5 and Table 8 shows the intoxication cases distributed by age in relation to the type of poisoning, in boys.

Figure 5- Distribution of intoxication cases by type of poisoning *versus* age, in males

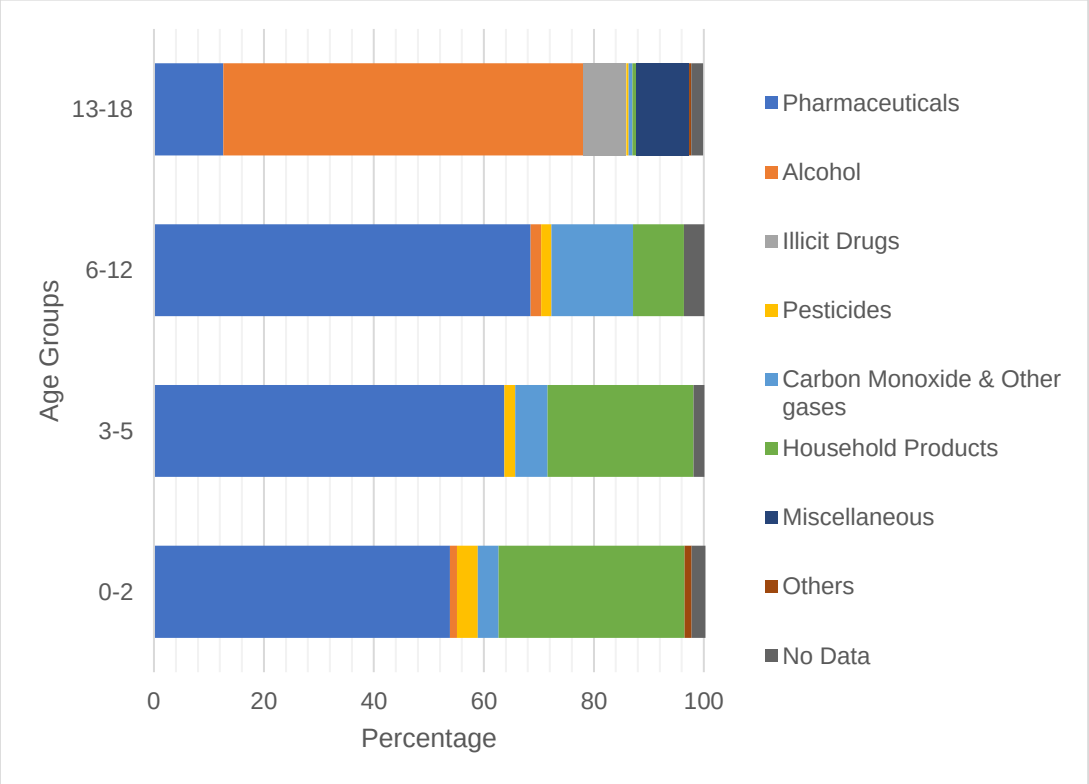


Table 8- Distribution of intoxication cases by type of poisoning *versus* age, in males

	Age groups (years)			
	≤2	3-5	6-12	13-18
	N (%)	N (%)	N (%)	N (%)
Pharmaceuticals	86 (53.8%)	65 (63.7%)	37 (68.5%)	56 (12.6%)
Alcohol	2 (1.3%)	0 (0.0%)	1 (1.9%)	292 (65.5%)
Illicit Drugs	0 (0.0%)	0 (0.0%)	0 (0.0%)	35 (7.8%)
Pesticides	6 (3.8%)	2 (2.0%)	1 (1.9%)	2 (0.4%)
Carbon Monoxide & Other gases	6 (3.8%)	6 (5.9%)	8 (14.8%)	3 (0.7%)
Household Products	54 (33.8%)	27 (26.5%)	5 (9.3%)	3 (0.7%)
Miscellaneuos	0 (0.0%)	0 (0.0%)	0 (0.0%)	43 (5.6%)
Others	2 (1.3%)	0 (0.0%)	0 (0.0%)	2 (0.4%)
No Data	4 (2.5%)	2 (2.0%)	2 (3.7%)	10 (2.2%)

The circumstances of intoxication were divided into two broad classes: intentional and accidental. Within the intentional group, we classified them into i) child neglect, ii) deliberate, iii) substance misuse-related poisoning; and iv) suicidal ideation. Therapeutic errors and accidents were attributed to non-intentional poisoning.

In table 9, it is possible to observe that poisonings with intention prevailed over accidental ones (1,017 cases *versus* 558 cases). In addition, intentional intoxication was predominant in the group of adolescents (984 cases; 97.1%), in contrast to the younger age groups (both in children aged ≤2 years and those aged between 3 and 5 years) which were represented by a higher number of accidents (464 cases; 98.9%) (p<0,001). In 9 cases, the intention was not established.

Regarding gender, there was a significant difference in younger children and teenagers (p<0,001). Therefore, boys accounted for most non-intentional poisonings – 158 (98.8%) and 101 (99%) cases in toddlers and pre-schoolers, correspondingly. Intentional intoxication was characteristic of girls – 550 cases in adolescents (97%).

Table 9- Intent by gender and age groups

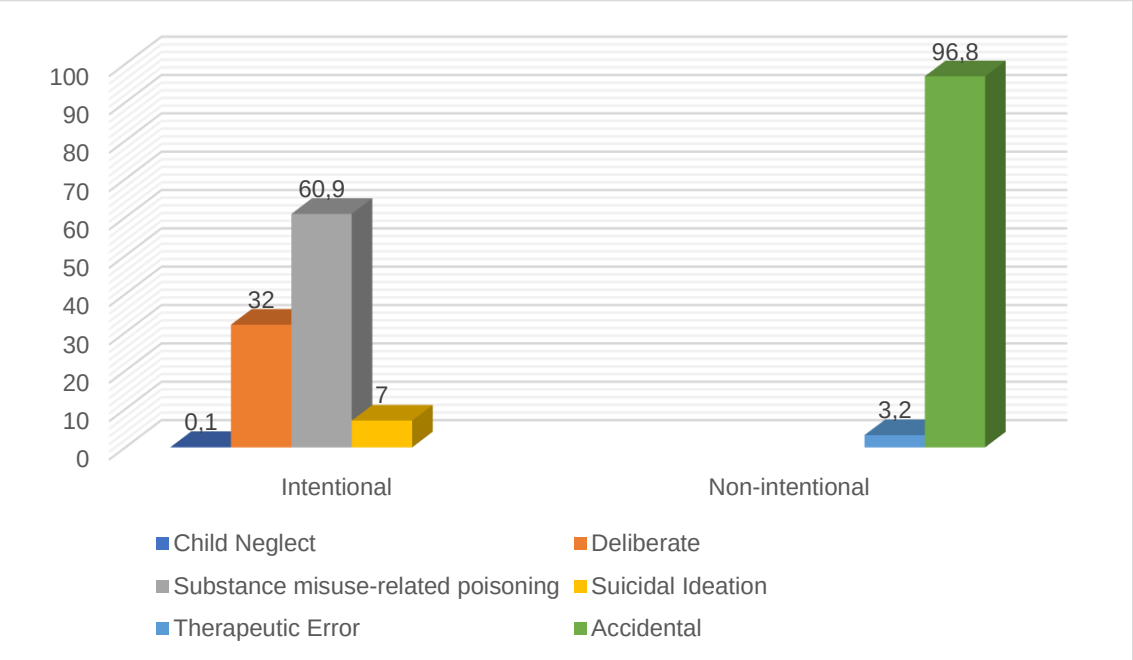
			AGE GROUPS (YEARS)				TOTAL
			≤2	3-5	6-12	13-18	
			N (%)	N (%)	N (%)	N (%)	N (%)
MALES	Intent	Non-intentional	158 (98.8)	101 (99.0)	40 (74.1)	9 (2.0)	308 (40.4)
		Intentional	2 (1.3)	1 (1.0)	11 (20.4)	434 (97.3)	448 (58.8)
		No data	0 (0.0)	0 (0.0)	3 (0.7)	3 (0.7)	6 (0.8)
FEMALES		Non-intentional	138 (98.6)	67 (100)	31 (64.6)	14 (2.5)	250 (30.4)
		Intentional	2 (1.4)	0 (0.0)	17 (35.4)	550 (97.0)	569 (69.2)
		No data	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.5)	3 (0.4))
TOTAL		Non-intentional	296 (98.7)	168 (99.4)	71 (69.6)	23 (2.3)	558 (35.2)
		Intentional	4 (1.3)	1 (0.6)	28 (1.8)	984 (97.1)	1,017 (64.2)
		No data	0 (0.0)	0 (0.0)	3 (2.9)	6 (0.6)	9 (0.6)

In intentional intoxications, 619 cases (60.9%) consisted of substance misuse-related poisoning (here were included cases related to the purposeful abuse of illicit substances or alcohol). The intentional use of the remaining classes of toxics was called deliberate, corresponding to 325 children poisonings (32%). Suicidal ideation corresponded to 72 cases (7%). There was also one case of child neglect (0.1%).

Accidental intoxication was prevalent in non-intentional poisoning with 540 paediatric cases (96.8%). The rest were due to therapeutic errors (18 cases; 3.2%) by the administration of the incorrect dose, drug or dosage (Figure 6).

As for the type of intoxication, pharmaceuticals (332 cases; 59.5%) and household products (143 cases; 25.6%) were the main toxic agents involved in accidents, compared to all other groups (p<0,001). In the case of intentional poisoning, in addition to pharmaceuticals (350 cases; 34.4%), alcohol was also high rated (516 cases; 50.7%).

Figure 6- Poisoning by specific intent



Of the 1,584 cases of paediatric poisoning, only 45 (2.8%) required hospitalizations. No infant deaths occurred. In addition, the most significant discharge place was home (1,130 cases; 71.3%), as we can see in Table 10. The remaining children (452 cases; 28.5%) had one of the following destinations: other hospital, primary care provider, discharge against medical advice, outpatient consultation, administrative discharge and admitted to hospital.

Table 10- Hospital admission data by age group

	Age groups (years)				Total
	≤2	3-5	6-12	13-18	
	N (%)	N (%)	N (%)	N (%)	N (%)
Home	265 (88.3)	156 (92.3)	81 (79.4)	628 (62.0)	1,130 (71.3)
Others	35 (11.7)	13 (7.7)	21 (20.6)	383 (37.8)	452 (28.5)
No data	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.1)

Regarding the moment of poisoning, the year 2014 had the maximum number of cases (262 cases; 16.5%), but this difference was not statistically significant (p<0.51). Most intoxicated children attend school (889 cases; 56.1%). The most prevalent season of the year corresponded to winter and spring with 410 (25.9%) and 406 cases (25.6%),

correspondingly. Compared to other week days, the highest number of intoxications was observed at the weekend (18.8% and 18.4% on Saturday and Sunday, respectively). Here we can emphasize the abusive use of alcohol and illegal drugs, which accounted for 171 (27.6%) and 152 (24.6%) cases during the weekend.

Analysing the month and day whose number of cases was elevated, June (179 cases;11.3%) and day 1 (108 cases; 6.8%) stand out. Of these cases, 99 (16%) and 78 (12.6%) were due to alcohol and illicit drug abuse. The dates with the highest cases of intoxication corresponded to 24/June (46 cases; 2.9%) and 01/January (42 cases; 2.7%).

We can highlight that a higher number of adolescents get intoxicated both on weekends (410 intoxications; p<0,003) and in the spring and winter seasons (267 cases; 26.5% and 261 cases; 25.8%, respectively). It was not possible to establish whether children aged ≤2 years were enrolled in an educational establishment, so it was not confirmed whether they were on school vacation (Table 11).

Table 11- Intoxication cases by the year, day of week, season and school holiday by age group

		Age groups (years)				**Total**
		≤2	3-5	6-12	13-18	
		N (%)	N (%)	N (%)	N (%)	N (%)
Year	2010	26 (8.7)	12 (7.1)	9 (8.8)	86 (8.5)	133 (8.4)
	2011	21 (7.0)	24 (14.2)	5 (4.9)	81 (8.0)	131 (8.3)
	2012	31 (10.3)	18 (10.7)	9 (8.8)	115 (11.4)	173 (10.9)
	2013	42 (14.0)	22 (13.0)	4 (3.9)	104 (10.3)	172 (10.9)
	2014	50 (16.7)	25 (14.8)	16 (15.7)	171 (16.9)	262 (16.5)
	2015	43 (14.3)	18 (10.7)	18 (17.6)	104 (10.3)	183 (11.6)
	2016	28 (9.3)	23(13.6)	18 (17.6)	130 (12.8)	199 (12.6)
	2017	30 (10.0)	15 (8.9)	8 (7.8)	99 (9.8)	152 (9.6)
	2018	29 (10.0)	12 (7.1)	15 (14.7)	123 (12.1)	179 (11.3)
Season	Spring	71 (23.7)	41 (24.3)	27 (26.5)	267 (26.4)	406 (25.6)
	Summer	74 (24.7)	45 (26.6)	17 (16.7)	250 (24.7)	386 (24.4)
	Fall	79 (26.3)	45 (26.6)	23 (22.5)	235 (23.2)	382 (24.1)
	Winter	76 (25.3)	38 (22.5)	35 (34.3)	261 (25.8)	410 (25.9)
Day of the week	Monday	48 (16.0)	26 (15.4)	18 (17.6)	124 (12.2)	216 (13.6)
	Tuesday	39 (13.0)	22 (13.0)	15 (14.7)	127 (12.5)	203 (12.8)
	Wednesday	34 (11.3)	24 (14.2)	16 (15.7)	104 (10.3)	178 (11.2)
	Thursday	45 (15.0)	21 (12.4)	11 (10.8)	99 (9.8)	176 (11.1)
	Friday	36 (12.0)	23 (13.6)	13 (12.7)	149 (14.7)	221 (14.0)
	Saturday	50 (16.7)	26 (15.4)	14 (13.7)	208 (20.5)	298 (18.8)
	Sunday	48 (16.0)	27 (16.0)	15 (14.7)	202 (19.9)	292 (18.4)
School holiday	Yes	0 (0.0)	49 (29.0)	24(23.5)	323 (31.9)	396 (25.0)
	No	0 (0.0)	120 (71.0)	78 (76.5)	690 (68.1)	889 (56.1)
	No data	300 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	300 (18.9)

Most administrations occurred by the oral route (1,385 cases; 87.4%; p<0.001), followed by inhalation (96 cases; 6.1%) and oral and inhalation (46 cases; 2.9%). It should

be noted that we could not obtain data from 54 paediatric poisonings. Pharmaceuticals and alcohol were the main toxic agents ingested orally (with a total of 677 cases; 48.9% and 519 cases; 37.5%, respectively).

5. Discussion

The number of paediatric poisonings in the CHSJ over 8 years corresponded to 1,584 cases, which is similar to several studies carried out in Europe such as Italy (Turin; 1,030 cases; 6-year study), Spain (Multicentre study; 1,749 cases; 9-year-study) and France (Bordeaux; 2,988 cases; 7-year study) (Berta et al., 2020; Lamireau et al., 2022; Santiago et al., 2019).

The most common type of intoxication was with pharmaceuticals, corresponding to a total of 685 cases (43.2%). In the youngest children (≤ 5 years old), pharmaceuticals were the biggest cause of intoxication (292 cases; 62.3%) followed by household products (132 cases; 28.1%). Alcohol was the most used toxic agent by adolescents (512 cases; 50.5%), followed by pharmaceuticals (331 cases; 32.7%). These results are similar to other studies, namely those from Ferranti et al. (2018), Matalová et al. (2019) and Yehya et al. (2020), who observed a bimodal distribution in relation to the class of pharmaceuticals, with greater significance in children ≤5 years and adolescents ≥13 years.

Azab et al (2016) and Ulseth et al (2022), in Cairo and Norway respectively, obtained different results from our study, where the pharmaceutical class was more common in teens (Azab et al., 2016; Ulseth et al., 2022). Abbas et al (2012), in Pakistan, found that pharmaceuticals, pesticides (organophosphates) and kerosene were the main causes of poisoning in young children (<5 years old) from 2006 to 2007 (Abbas et al., 2012). Still, there are investigations whose trends agree with ours. In Taiwan, the predominant intoxicant class among younger children (<5 years old) was pharmaceuticals (187 cases; 81.3%) (Lee et al., 2019); in Poland, adolescents (≥13 years) and young children (≤5 years) used alcohol and pharmaceuticals as the main toxicants, respectively (Pac-Kozuchowska et al., 2016; Pawłowicz et al., 2013); in Mato Grosso (Brazil), pharmaceuticals were the major source of poisoning in children (up to 14 years of age) (F. F. S. Oliveira & Suchara, 2014) and in Italy, children ≥9 years of age were subjected to higher rates of intoxication by pharmaceuticals, followed by household products (Berta et al., 2020).

In our study, the pharmaceutical classes with the highest number of cases correspond to drugs that act on the CNS (324 cases; 47.3%), with predominance of anxiolytics, sedatives, and hypnotics (177 cases; 54.6%), where benzodiazepines can be highlighted; antidepressants (43 cases; 13.3%) and antipsychotics (39 cases; 12%). The analgesic and antipyretic group followed with 79 cases (11.5%) and antihistaminics with 66 cases (9.6%). In addition, 82 (12%) paediatric poisonings occurred due to the administration of the combination of several classes of pharmaceuticals. This result agrees with the literature, whose most prevalent children intoxication groups in Europe and the US were

psychotropics (antipsychotics and anxiolytics, sedatives and hypnotics), analgesics, antihistaminics and NSAIDs (Albertson et al., 2004; Berta et al., 2020; Greene et al., 2005; Hoikka et al., 2013; Koh et al., 2018; Matalová et al., 2019; Yehya et al., 2020).

Alcohol followed pharmaceuticals with 519 cases (32.8%). This high number might be due not only to the increase in alcohol consumption among minors, but also to binge drinking (Pawłowska-Kamieniak et al., 2018; Pianca et al., 2017; Schulte et al., 2009). It should be noted that there was a case of intoxication by alcohol at 70º in a 2-year-old boy. This fact was also observed by Gaw & Osterhoudt (2019) and Pawłowska-Kamieniak et al (2018), who emphasized the occurrence of accidental poisoning because it is ubiquitous in various products and foods, as well as easily accessible at home (Gaw & Osterhoudt, 2019; Pawłowska-Kamieniak et al., 2018).

Pesticides accounted for 14 cases (0.9%), with the vast majority occurring in 2014. The most common toxic agent was rodenticide. These products were, formerly, the cause of a large number of poisonings and since they are marketed and regulated by various laws in Portugal, such as Decree-Law no. 144/2004 and Decree-Law no. 140/2017, the number of intoxications has decreased. This demonstrates the effectiveness of laws and competent authorities in controlling these toxic agents.

Regarding the gender differences, we were able to obtain similar results, mentioned below, to other studies (Azab et al., 2016; Becker & Correll, 2020; Berta et al., 2020; Lamireau et al., 2022; Nistor et al., 2017; Pac-Kozuchowska et al., 2016). Accidental intoxications tend to occur mostly in males (308 *versus* 250 females), while intentional poisoning is more recurrent in females (569 *versus* 448 boys). In the age group ≤2 years old and pre-schoolers, accidental intoxication was more prevalent in boys (259 cases; 56%). This fact agrees with the literature (Abbas et al., 2012; Ahmed et al., 2015; Berta et al., 2020; Brito & Martins, 2015; Hassan & Siam, 2014; Lamireau et al., 2022; Pac-Kozuchowska et al., 2016), which indicates a predominance of accidents in children ≤ 6 years and males. On the other hand, in the adolescent group (from 13 to 18 years old), females suffered most of the intentional poisonings (550 cases; 97%), which is also in agreement with other studies (Azab et al., 2016; Gokalp, 2019; Hassan & Siam, 2014). These results can be explained by the fact that women are more prone to emotional behaviours, therefore they have a higher risk to psychiatric illnesses, such as depression and suicidal ideation, using less violent methods to comite suicide, compared to men (Azab et al., 2016; Becker & Correll, 2020). Furthermore, boys, even at early ages, have riskier behaviours and are more active, which constitutes a superior risk of accidents (Ahmed et al., 2015; Albertson et al., 2004; Greene et al., 2005; Pac-Kozuchowska et al., 2016).

Nistor et al (2017) did research, in Romania, during 2014, were stated that females tend to get intoxicated by medicines, while the most common methods of intoxication in males are alcohol and illicit drugs. In our study, these high trends were also confirmed: 295 (38.7%) alcohol intoxications and 441 (53.6%) pharmaceutical poisonings occurred in males and females, respectively (Azab et al., 2016; Becker & Correll, 2020; Nistor et al., 2017). In what concerns alcohol abuse, this difference is due to the different cultural and social norms to which each gender is subject, as girls are more supervised and punished and must follow standardized rules by society and family (Schulte et al., 2009). In addition to the fact mentioned above, the greater consumption of alcohol in boys may be due to the bigger sensitivity of females to alcohol, the social repercussions, and the higher danger of physical and sexual aggression (Schulte et al., 2009).

In females, as previously mentioned, pharmaceuticals were the most common intoxication class, in particular drugs that act essentially on the CNS. Accordingly, 220 paediatric poisonings were observed by medicines acting on the CNS such as anxiolytics, sedatives and hypnotics (123 *versus* 54 boys), antidepressants (34 *versus* 14 boys) and antipsychotics (22 *versus* 17 boys).

Relative to age, it is possible to observe a predominance of poisoning in adolescence (1,013 cases; 64.0%). The same occurred in a study carried out in Poland (2006-2010), where 76.9% were teenagers. (Pawłowicz et al., 2013). This result differs from other studies, where the peak number of cases occurred in children ≤ 5 years (Abbas et al., 2012; Ahmed et al., 2015; Berta et al., 2020; Hassan & Siam, 2014; Hoikka et al., 2013; Koh et al., 2018; F. F. S. Oliveira & Suchara, 2014; Schmertmann et al., 2013). This may be due to the growing consumption of alcohol at increasingly younger ages (from 14 years old up), since it corresponds to one of the substances most ingested by teens - 512 cases (50.5%). A study carried out in Portugal between 2012 and 2016 with intoxicated patients whose ages ranged from 10 to 17 years, showed that the average age of alcohol consumption was 15.9 years (Rodrigues et al., 2018). Allied to this, binge drinking exponentially increased leading often to intoxication (Pawłowska-Kamieniak et al., 2018; Pianca et al., 2017; Schulte et al., 2009).

Intentional poisoning had a total of 1,017 cases (64.2%) while accidental intoxication only accounted for 558 cases (35.2%). This is also consistent with the fact that our population is mainly constituted by teenagers. Thus, the intentional character predominated in the age group of adolescents (984 cases; 97.1%) and the accidents in children aged ≤5 years (464 cases; 83.1%), which coincides with the literature (Albertson et al., 2004; Berta et al., 2020; Lamireau et al., 2022; Nistor et al., 2017; F. F. S. Oliveira & Suchara, 2014;

Pac-Kozuchowska et al., 2016; Schmertmann et al., 2013; Vilaça et al., 2020). This inequality observed is due to the typical behaviour of young children in relation to the environment, since they tend to be curious about colourful products, explore the environment and have a strong oral orientation (Abbas et al., 2012; Ahmed et al., 2015; Albertson et al., 2004; Berta et al., 2020; Brito & Martins, 2015; Hassan & Siam, 2014; Hoikka et al., 2013; Koh et al., 2018; F. F. S. Oliveira & Suchara, 2014; Pac-Kozuchowska et al., 2016; Schmertmann et al., 2013). In adolescence, several psychophysical changes occur, and the social factor becomes imperative during this phase, both in the family and school environments, leading to substance abuse and suicidal ideation (Albertson et al., 2004; Berta et al., 2020; Lamireau et al., 2022; Nistor et al., 2017; F. F. S. Oliveira & Suchara, 2014; Pac-Kozuchowska et al., 2016).

Therapeutic errors corresponded to 1.1% (18 cases) of the total, occurring mainly in the age group from 6 to 12 years (10 cases; 55.6%); and accounts for 3.2% of unintentional intoxications. This fact agrees with the literature, in which cases may reach up to 5% of accidental poisonings (Dayasiri et al., 2020; von Fabeck et al., 2020).

We must highlight one case of child neglect. The male child was 5 years old and ingested 1 tablet of oxazepam (benzodiazepine) on the recommendation of the mother who had psychiatric problems. These types of disorders constitute a factor of negligence as the mother becomes incapable or barely able to answer the child's basic needs, whether physical, medical, educational, or emotional (Gaw & Osterhoudt, 2019).

However, it was not possible to determine the intention of intoxication in 9 cases.

The paediatric population studied presented only mild symptoms or no symptoms at all, which makes the number of cases of hospitalization low (45 cases; 2.8%) and the home as the main place of discharge. In addition, no deaths occurred in our study.

Most paediatric poisonings occurred during school hours (889 cases; 56.1%), mainly during winter and spring. Lee et al (2019), in Taiwan, obtained 28% and 26.1% cases occurring in winter and spring, respectively (5-year study) and Pawłowicz et al (2013) also found that the frequency of intoxication increased during school period and decreased in summer (Lee et al., 2019; Pawłowicz et al., 2013). The year 2014 was the most prevalent. Saturday and Sunday were the days with the highest number of cases, which can be explained by the school break and leisure period, when children and adolescents can spend more time with no supervision. Adding the fact that teenagers were the most prevalent age group, socialization (including engaging in alcohol and illegal drugs with peers) occurs mainly during the weekend, festivities, and New Year's Eve (Albertson et al., 2004). We

verified this fact by obtaining the higher number of cases in 24/June (46 cases; 2.9%) and 01/January (42 cases; 2.7%), whose dates correspond to New Year and Saint John's Day.

The most frequent route of exposure, in all groups, was the oral route, as observed in other studies (Berta et al., 2020; Hassan & Siam, 2014; Lee et al., 2019; Vilaça et al., 2020). However, there were 54 cases (3.4%) in which it was not possible to determine the route of exposure due to lack of information.

6. Conclusions

Between 2010 and 2018, 1,584 paediatric intoxications were admitted in CHSJ, especially in children under 5 years of age and adolescents. Pharmaceuticals were more common among teens girls, while alcohol was the substance most consumed by adolescent males. For younger children, household products and pharmaceuticals were the most prevalent. This reveals the need to implement cautious measures in the storage and security of pharmaceuticals and household products, as well as improved methods and laws to control the supply of alcohol and medicines to children. It should be noted that intoxications are mostly intentional in adolescents and accidental in younger ones. No deaths occurred during the 8 years and intoxication symptoms were mostly mild or moderate.

According to data provided by the Poison Information Center (CIAV) on poisoning, the prevalence of poisoning in children peaks between 1 and 4 years of age, with a predominance of males (Serviço Nacional de Saúde, 2020). These data agree with one of our study main trends, related to accidental intoxications. It is possible that CIAV is nor requested as often since it is a centre whose objective is to provide information on intoxications, and adolescents (the group with the highest number of cases) do not intend to use this service to seek information on alcohol (the main toxic involved).

In 2020, CIAV carried out 27,287 medical consultations, of which 6,432 cases corresponded to accidental poisoning in children. The main toxic agent involved were pharmaceuticals. This result was also confirmed by our study. The total number of calls was slightly lower than in other years due to the COVID-19 pandemic (Serviço Nacional de Saúde, 2020).

The biggest limitation of this article is the lack of information on the cases presented, including on the amount of toxic, identification of the intoxicating agent, and the circumstances of intoxication. In addition, in some cases, the ICD-9 diagnosis was incorrect (both in the toxic agent class and the characterization of intent). With this, it becomes necessary to provide good quality information in medical reports not only to obtain a correct diagnosis and treatment, but also to enable the performance of different types of studies. The greatest strength corresponds to the large sample and the availability of data.

This study only focused on one region of the country, Porto, so further research should be carried out in different parts of the country, to clarify whether the results found in the north of Portugal translate at a national level. With this, several measures can be implemented to reduce the number of paediatric cases diagnosed with intoxication. These interventions should be multidimensional, involving educational, regulatory and policy

approaches such as: developing public awareness programs about poisonings for health professionals, parents and the community; improve emergency unit response plans to reduce exposure time; increase legal approaches to drug control and strengthen the ethical responsibilities of farmers, healthcare professionals and retailers regarding the need to advise customers on the safe use and storage of products they dispense.

7. Bibliography

Abbas, S., Tikmani, S., & Siddiqui, N. (2012). Accidental poisoning in children. *J Park Med Assoc*, *62*(4), 331–334.

Abdel Baseer, K. A., Gad, E. F., & Abdel Raheem, Y. F. (2021). Clinical profile and outcome of acute organophosphate poisoning in children of Upper Egypt: a cross-sectional study. *BMC Pediatrics*, *21*(1).

Agarwal, M., Lovegrove, M. C., Geller, R. J., Pomerleau, A. C., Sapiano, M. R. P., Weidle, N. J., Morgan, B. W., & Budnitz, D. S. (2020). Circumstances Involved in Unsupervised Solid Dose Medication Exposures among Young Children. *Journal of Pediatrics*, *219*, 1–8.

Ahmadi, A., Pakravan, N., & Ghazizadeh, Z. (2010). Pattern of acute food, drug, and chemical poisoning in Sari City, Northern Iran. *Human and Experimental Toxicology*, *29*(9), 731–738.

Ahmed, A., AlJamal, A. N., Mohamed Ibrahim, M. I., Salameh, K., AlYafei, K., Zaineh, S. A., & Adheir, F. S. S. S. (2015). Poisoning emergency visits among children: A 3-year retrospective study in Qatar. *BioMed Central Pediatrics*, *15*(104), 1–7.

Albertson, T., Alsop, J., Anderson, Ii., Balmes, J., Banerji, S., Barry, J., & Benowitz, N. (2004). *Poisoning & drug overdose* (Vol. 4). Lange Medical Books/McGraw-Hill.

Alinejad, S., Zamani, N., Abdollahi, M., & Mehrpour, O. (2017). A Narrative Review of Acute Adult Poisoning in Iran. *Iran J Med Sci*, *42*(4), 327–346.

Alotaibi, N., Sammons, H., & Choonara, I. (2012). Methadone toxicity in children. *Archives of Disease in Childhood*, *97*(5).

Azab, S. M. S., Hirshon, J. M., Hayes, B. D., El-Setouhy, M., Smith, G. S., Sakr, M. L., Tawfik, H., & Klein-Schwartz, W. (2016). Epidemiology of acute poisoning in children presenting to the poisoning treatment center at Ain Shams University in Cairo, Egypt, 2009-2013. In *Clinical Toxicology* (Vol. 54, Issue 1, pp. 20–26). Taylor and Francis Ltd.

Azkunaga, B., Crespo, E., Oliva, S., Humayor, J., & Mangione, L. (2017). Poisoning by illegal drugs in young children in Spanish paediatric emergency departments. *Anales de Pediatría* , *86*(1), 47–49.

Banerji, S., & Anderson, I. B. (2001). Abuse of Coricidin HBP Cough & Cold tablets: Episodes recorded by a poison center. *Am J Health-Syst Pharm*, 1811–1818.

Becker, M., & Correll, C. U. (2020). Suicidality in childhood and adolescence. In *Deutsches Arzteblatt International* (Vol. 117, Issue 15, pp. 261–267). Deutscher Arzte-Verlag GmbH.

Berta, G. N., di Scipio, F., Bosetti, F. M., Mognetti, B., Mognetti, B., Romano, F., Carere, M. E., del Giudice, A. C., Castagno, E., Bondone, C., & Urbino, A. F. (2020). Childhood acute poisoning in the Italian North-West area: A six-year retrospective study. *Italian Journal of Pediatrics*, *46*(83), 1–9.

Bitunjac, K., & Saraga, M. (2009). Alcohol intoxication in Pediatric age: Ten-year retrospective study. *Croatian Medical Journal*, *50*(2), 151–156.

Bouthoorn, S. H., van Hoof, J. J., & van der Lely, N. (2011). Adolescent alcohol intoxication in Dutch hospital centers of pediatrics: Characteristics and gender differences. *European Journal of Pediatrics*, *170*(8), 1023–1030.

Brito, J. G., & Martins, C. B. de G. (2015). Accidental intoxication of the infant-juvenile population in households: Profiles of emergency care. *Revista Da Escola de Enfermagem*, *49*(3), 372–379.

Caksenl, H., Akbayram1, S., Odaba, D., Özbek2, H., Erol1, M., Akgün1, C., Tuncer1, O., & Yllmaz', C. (2006). Acute amitriptyline intoxication: an analysis of 44 children. *Human & Experimental Toxicology*, *25*, 107–110.

Calabuig, G. (2004). *Medicina legal y toxicologia* (Vol. 6).

Chen, Y. C., & Klig, J. E. (2019, June 1). Cannabis-related emergencies in children and teens. *Current Opinion in Pediatrics*, *31*(3), 291–296.

Cho, C. H., Chiu, N. C., Ho, C. S., & Peng, C. C. (2008). Carbon Monoxide Poisoning in Children. *Pediatrics and Neonatology*, *49*(4), 121–125.

Christensen, G. M., Creswell, P. D., & Meiman, J. G. (2019). Carbon Monoxide Exposure and Poisoning Cases in Wisconsin, 2006-2016. *Wisconsin Medical Journal*, *118*(1), 21–26.

Chung, E. Y., & Tat, S. T. (2016). Nonsteroidal Anti-Inflammatory Drug Toxicity in Children A Clinical Review. *Pediatric Emergency Care*, *32*(4), 250–255.

Claudet, I., le Breton, M., Bréhin, C., & Franchitto, N. (2017). A 10-year review of cannabis exposure in children under 3-years of age: do we need a more global approach? *European Journal of Pediatrics*, *176*(4), 553–556.

Coben, J. H., Davis, S. M., Furbee, P. M., Sikora, R. D., Tillotson, R. D., & Bossarte, R. M. (2010). Hospitalizations for Poisoning by Prescription Opioids, Sedatives, and Tranquilizers. *American Journal of Preventive Medicine*, *38*(5), 517–524.

Creswell, P. D., Gibson, C., Theobald, J., & Meiman, J. G. (2019). Exposures to Opioids Among Wisconsin Children and Adolescents, 2002-2016. *Wisconsin Medical Journal*, *118*(1), 9–15.

Dayasiri, K., Jayamanne, S. F., & Jayasinghe, C. Y. (2020). Accidental and Deliberate Self-Poisoning with Medications and Medication Errors among Children in Rural Sri Lanka. *Emergency Medicine International*, *2020*, 1–8.

Detsouli, A., Amiar, L., Nabih, Z., Kharbouch, D., Windy, M., Rhalem, N., Soulaymani, A., Mokhtari, A., & Soulaymani- Bencheikh, R. (2017). Epidemiology of acute pesticide poisoning in Morocco: A 7-year retrospective study (2008-2014). *Journal of Materials and Environmental Science*, *8*(12), 4234–4239.

Domingos, S. M., Borghesan, N. B. A., Merino, M. de F. G. L., & Higarashi, I. H. (2016). Internações por intoxicação de crianças de zero a 14 anos em hospital de ensino no Sul do Brasil, 2006-2011. *Epidemiologia e Servicos de Saude*, *25*(2), 343–350.

Eifinger, F., Roth, B., Kröner, L., & Rothschild, M. A. (2008). Severe Ecstasy poisoning in an 8-month-old infant. *European Journal of Pediatrics*, *167*(9), 1067–1070.

Elenga, N., Merlin, C., le Guern, R., Kom-Tchameni, R., Ducrot, Y. M., Pradier, M., Ntab, B., Dinh-Van, K. A., Sobesky, M., Mathieu, D., Dueymes, J. M., Egmann, G., Kallel, H., & Mathieu-Nolf, M. (2018). Clinical features and prognosis of paraquat poisoning in French Guiana. *Medicine* , *97*(15), 1–7.

Farnaghi, F., Gholami, N., Hassanian-Moghaddam, H., McDonald, R., Zamanzadeh, R., & Zamani, N. (2021). Unintentional buprenorphine and methadone poisoning in children: a matched observational study. *Clinical Toxicology*, *59*(8), 1–7.

Ferranti, S., Grande, E., Gaggiano, C., & Grosso, S. (2018). Antiepileptic drugs: Role in paediatric poisoning. In *Journal of Paediatrics and Child Health* (Vol. 54, Issue 5, pp. 1–5). Blackwell Publishing.

Fonseca, D. A., Ribeiro, D. M., Tapadas, M., & Cotrim, M. D. (2021). Ecstasy (3,4-methylenedioxymethamphetamine): Cardiovascular effects and mechanisms. In *European Journal of Pharmacology* (Vol. 903, pp. 1–10). Elsevier B.V.

Fook, S., Azevedo, E., Costa, M., Feitosa, I., Bragaganoli, G., & Mariz, S. (2013). Poisoning with household cleaning products in a city in Northeast Brazil. *Cad. Saúde Pública*, *29*(5), 1041–1045.

Franchitto, N. (2020). Buprenorphine poisoning in children: a 10-year experience of Marseille Poison Center. In *Fundamental and Clinical Pharmacology* (Vol. 34, Issue 2, pp. 263–264). Blackwell Publishing Ltd.

Garland, J., Smith, D., Rice, T., & Siker, D. (1989). Accidental cocaine intoxication in a nine-month-old infant: Presentation and treatment. *Pediatric Emergency Care*, *5*(4), 245–247.

Gaw, C. E., & Osterhoudt, K. C. (2019). Ethanol Intoxication of Young Children. *Pediatric Emergency Care*, *35*(10), 722–730.

Ge, W., Wang, H. L., & Sun, R. P. (2014). Clinical characteristics of paraquat poisoning in 22 Chinese children. *Indian Journal of Pediatrics*, *81*(7), 670–674.

Ge, W., Wang, H. L., & Sun, R. P. (2014). Clinical characteristics of paraquat poisoning in 22 Chinese children. *Indian Journal of Pediatrics*, *81*(7), 670–674.

Geulayov, G., Ferrey, A., Casey, D., Wells, C., Fuller, A., Bankhead, C., Gunnell, D., Clements, C., Kapur, N., Ness, J., Waters, K., & Hawton, K. (2018). Relative toxicity of benzodiazepines and hypnotics commonly used for self-poisoning: An epidemiological study of fatal toxicity and case fatality. *Journal of Psychopharmacology*, *32*(6), 1–9.

Gokalp, G. (2019). Evaluation of poisoning cases admitted to pediatric emergency department. *International Journal of Pediatrics and Adolescent Medicine*, *6*(3), 109–114.

Goudarzi, M., Eizadi-Mood, N., Mansourian, M., Mohammadi-Jouabadi, S., Peymani, P., & Sabzghabaee, A. (2020). Pediatric toxicoepidemiology of tramadol intoxication in Iran: A 5-year cross-sectional study. *Journal of Research in Pharmacy Practice*, *9*(1), 44–49.

Graham, J., Leonard, J., Banerji, S., & Wang, G. S. (2020). Illicit Drug Exposures in Young Pediatric Patients Reported to the National Poison Data System, 2006-2016. *Journal of Pediatrics*, *219*, 254-258.

Graudins, A., & Fern, R. P. (1996). Acute dystonia in a child associated with therapeutic ingestion of a dextromethorphan containing cough and cold syrup. *Clinical Toxicology*, *34*(3), 351–352.

Greene, S. L., Dargan, P. I., & Jones, A. L. (2005). Acute poisoning: Understanding 90% of cases in a nutshell. In *Postgraduate Medical Journal* (Vol. 81, Issue 954, pp. 204–216).

Hassan, B. A., & Siam, M. G. (2014). Patterns of Acute Poisoning in Childhood in Zagazig, Egypt: An Epidemiological Study. *International Scholarly Research Notices*, *2014*, 1–5.

Hoikka, M. H., Liisanantti, J. H., & Dunder, T. (2013). Acute poisoning in children under the age of six: A two-decade study of hospital admissions and trends. *Acta Paediatrica, International Journal of Paediatrics*, *102*(7), 329–333.

Joseph Judge, D., & DUMARS Jr, K. W. (1953). Diphenhydramine (benadryl) and tripelennamine (pyribenzamine) intoxication in children. *American Journal of Diseases of Children*, *142*(2), 545–550.

Jung, Y. chul, & Namkoong, K. (2014). Alcohol: Intoxication and poisoning - diagnosis and treatment. In *Handbook of Clinical Neurology* (Vol. 125, pp. 115–121). Elsevier B.V.

Kamińska, H., Gawlik, A., Gawlik, T., & Małecka-Tendera, E. (2018). Hospitalizations due to alcohol intoxication among children and adolescents – a report from a single-center retrospective study. *Psychiatria Polska*, *52*(2), 387–398.

Karapirli, M., Kandemir, E., Akyol, S., Kantarci, M. N., Kaya, M., & Akyol, O. (2013). Forensic and clinical carbon monoxide (CO) poisonings in Turkey: A detailed analysis. *Journal of Forensic and Legal Medicine*, *20*(2), 95–101.

King, A. M., & Aaron, C. K. (2015). Organophosphate and Carbamate Poisoning. In *Emergency Medicine Clinics of North America* (Vol. 33, Issue 1, pp. 133–151). W.B. Saunders.

Kizilyildiz, B. S., Karaman, K., Ozen, S., & Uner, A. (2018). Acute intoxications among Turkish children. *Minerva Pediatrica*, *70*(1), 46–50.

Koh, S. H., Tan, K. H. B., & Ganapathy, S. (2018). Epidemiology of paediatric poisoning presenting to a children's emergency department in Singapore over a five-year period. *Singapore Medical Journal*, *59*(5), 247–250.

Krakowiak, A., Bak, M., Politanski, P., & Piekarska-Wijatkowska, A. (2020). Clinical pattern of poisoning among patients declared as taking novel recreational drugs. *International Journal of Occupational Medicine and Environmental Health*, *33*(4), 445–455.

Kuželová, M., Harárov, A., Ondriašová, E., Wawruch, M., Riedel, R., Benedeková, M., Kovács, L., & Plakov, S. (2009). Alcohol intoxication requiring hospital admission in children and adolescents: Retrospective analysis at the University Children's Hospital in the Slovak Republic. *Clinical Toxicology*, *47*(6), 556–561.

Lamireau, T., Llanas, B., Kennedy, A., Fayon, M., Penouil, F., Favarell-Garrigues, J.-C., & Demarquez, J.-L. (2022). Epidemiology of poisoning in children: a 7-year survey in a paediatric emergency care unit. *European Journal of Emergency Medicine*, *9*, 9–14.

Lee, J., Fan, N. C., Yao, T. C., Hsia, S. H., Lee, E. P., Huang, J. L., & Wu, H. P. (2019). Clinical spectrum of acute poisoning in children admitted to the pediatric emergency department. *Pediatrics and Neonatology*, *60*(1), 59–67.

Liffhitz, M., Shahak, E., & Sofer, S. (1999). Carbamate and organophosphate poisoning in young children. *Pediatric Emergency Care*, *15*(2), 102–103.

Magera, B., Betlach, C., & Sweatt, A. (1981). *Hydroxyzine intoxication in a 13-month-old child*. Pediatrics.

Magnani, B., & Evans, R. (1999). Codeine Intoxication in the Neonate. *Pediatrics*, *104*(6), 1–3.

Malangu, N. (2008). Acute poisoning at two hospitals in Kampala-Uganda. *Journal of Forensic and Legal Medicine*, *15*(8), 489–492.

Matalová, P., Poruba, M., Wawruch, M., Ondra, P., & Urbánek, K. (2019). Acute medication poisoning causing hospital admissions in childhood: A 3-year prospective observational single-center study. *Physiological Research*, *68*, 31–38.

Melian, A. M., Burillo-Putze, G., Gonzalez Campo, C., Gonzalez Padron, A., & Ramos, C. O. (2004). Accidental Ecstasy Poisoning in a Toddler. *Pediatric Emergency Care*, *20*(8), 534–535.

Mintegi, S., Fernández, A., Alustiza, J., Canduela, V., Mongil, I., Caubet, I., Clerigué, N., Herranz, M., Crespo, E., Fanjul, J. L., Fernández, P., Humayor, J., Landa, J., Muñoz, J. A., Lasarte, J. R., Núñez, F. J., López, J., Molina, J. C., Pérez, A., … Vázquez, P. (2006). Emergency Visits for Childhood Poisoning: A 2-Year Prospective Multicenter Survey in Spain. *Pediatric Emergency Care*, *22*(5), 334–338.

Mott, S., Packer, R., & Soldin, S. (1994). *Neurologic manifestations of cocaine exposure in childhood - PubMed*. Pediatrics.

Müller, D., & Desel, H. (2013). Common causes of poisoning: Etiology, diagnosis and treatment. *Deutsches Arzteblatt International*, *110*(41), 690–700.

Ng, P. C., Banerji, S., Graham, J., Leonard, J., & Wang, G. S. (2019). Adolescent exposures to traditional and novel psychoactive drugs, reported to National Poison Data System (NPDS), 2007–2017. *Drug and Alcohol Dependence*, *202*, 1–5.

Nistor, N., Jitareanu, C., Frasinariu, O. E., Ciomaga, I. M., Rugina, A. L., & Streanga, V. (2017). Epidemiologic profile and triggering factors of voluntary poisoning in teenagers. *Medicine* , *96*(5), 1–5.

Oliveira, F. F. S., & Suchara, E. A. (2014). Epidemiological profile of exogenous poisoning in children and adolescents from a municipality in the state of Mato Grosso. *Revista Paulista de Pediatria*, *32*(4), 299–305.

Oliveira, M., & Arnauts, I. (2011). Intoxicação alcoólica em crianças e adolescentes: dados de um centro de assistência toxicológica. *Escola Anna Nery*, 83–89.

Oral, R., Bayman, L., Assad, A., Wibbenmeyer, L., Buhrow, J., Austin, A., & Bayman, E. O. (2011). Illicit Drug Exposure in Patients Evaluated for Alleged Child Abuse and Neglect Background: Substantiation of drug exposure in cases with alleged. *Pediatric Emergency Care*, *27*(6), 490–495.

Pac-Kozuchowska, E., Krawiec, P., Mroczkowska-Juchkiewicz, A., Mełges, B., Pawłowska-Kamieniak, A., Kominek, K., & Gołyska, D. (2016). Patterns of poisoning in urban and rural children: A single-center study. *Advances in Clinical and Experimental Medicine*, *25*(2), 335–340.

Parker-Cote, J. L., Rizer, J., Vakkalanka, J. P., Rege, S. v., & Holstege, C. P. (2018). Challenges in the diagnosis of acute cyanide poisoning. In *Clinical Toxicology* (Vol. 56, Issue 7, pp. 1–8). Taylor and Francis Ltd.

Pauwels, S., Lemmens, F., Eerdekens, K., Penders, J., Poesen, K., Desmet, K., & Vermeersch, P. (2013). Ecstasy intoxication as an unusual cause of epileptic seizures in young children. *European Journal of Pediatrics*, *172*(11), 1547–1550.

Pawłowicz, U., Wasilewska, A., Nski, W. O., & Stefanowicz, M. (2013). Epidemiological study of acute poisoning in children: a 5-year retrospective study in the Paediatric University Hospital in Białystok, Poland. *Emerg Med J*, *30*, 712–716.

Pawłowska-Kamieniak, A., Mroczkowska-Juchkiewicz, A., Kominek, K., Krawiec, P., Mełges, B., & Pac-Kożuchowska, E. (2018). Alcohol intoxication among adolescents and children in urban and rural environments – A retrospective analysis. *Annals of Agricultural and Environmental Medicine*, *25*(1), 1–3.

Pianca, T. G., Sordi, A. O., Hartmann, T. C., & von Diemen, L. (2017). Identification and initial management of intoxication by alcohol and other drugs in the pediatric emergency room. In *Jornal de Pediatria* (Vol. 561, pp. 1–7). Elsevier Editora Ltda.

Qiu, L., & Deng, Y. (2019). Paraquat Poisoning in Children A 5-Year Review. *Pediatric Emergency Care*, 1–4.

Rayar, P., & Ratnapalan, S. (2013). Pediatric ingestions of house hold products containing ethanol: A review. *Clinical Pediatrics*, *52*(3), 203–209.

Rijswijk, C. W. E., Kneyber, M. C. J., & Plötz, F. B. (2006). Accidental ecstasy intoxication in an 8-month-old infant. In *Intensive Care Medicine* (Vol. 32, Issue 4, pp. 632–633).

Roberts, J. R., Karr, C. J., Paulson, J. A., Brock-Utne, A. C., Brumberg, H. L., Campbell, C. C., Lanphear, B. P., Osterhoudt, K. C., Sandel, M. T., Trasande, L., & Wright, R. O. (2012). Pesticide Exposure in Children. *Pediatrics*, *130*(6), 1765–1788.

Rodrigues, M., Pontes, T., Almeida, J., Estrada, A., & Carvalho, S. (2018). Alcohol use in adolescence: 5 years admissions at a pediatric emergency department. *International Journal of Adolescent Medicine and Health*, *32*(4), 1–7.

Ryan, S. (2019, December 1). Cocaine Use in Adolescents and Young Adults. *Pediatric Clinics of North America*, *66*(6), 1135–1147.

Samuelsson, B. (1974). Lsd intoxication in a two-year-old child. *Acta Pzdiatr Scand*, *63*, 797–798.

Santiago, P., Bilbao, N., Martinez-Indart, L., Mintegi, S., & Azkunaga, B. (2019). Epidemiology of acute pediatric poisonings in Spain: A prospective multicenter study from the Spanish Society of Pediatric Emergency Medicine. *European Journal of Emergency Medicine*, 1–6.

Santos, R. R. dos, Machado, M. E. D., Gomes, A. L. M., Aguiar, R. C. B. de, & Christoffel, M. M. (2021). Prevenção de acidentes domésticos na infância: conhecimento de cuidadores em uma unidade de saúde. *Revista Brasileira de Enfermagem*, *75*(2), 1–8.

Sawicka, E., Kartuszyńska, P., Kuczyńska, H., & Piwowar, A. (2019). A retrospective observational study on patients intoxicated by drugs and other xenobiotics. *International Journal of Occupational Medicine and Environmental Health*, *32*(4), 489–501.

Schmertmann, M., Williamson, A., Black, D., & Wilson, L. (2013). Risk factors for unintentional poisoning in children aged 1-3 years in NSW Australia: A case-control study. *BioMed Central Pediatrics*, *13*(88), 1–15.

Schulte, M. T., Ramo, D., & Brown, S. A. (2009). Gender differences in factors influencing alcohol use and drinking progression among adolescents. In *Clinical Psychology Review* (Vol. 29, Issue 6, pp. 535–547).

Schwebel, D. C., Wells, H., & Johnston, A. (2015). Children's recognition of dangerous household products: Child development and poisoning risk. *Journal of Pediatric Psychology*, *40*(2), 238–250.

Serviço Nacional de Saúde. (2020). *Relatório Anual Atividades Específicas desenvolvidas nos Centros de Orientação de Doentes Urgentes (CODU)*.

Sharma, N., & Nin-Gonzalez, R. (2021). Organophosphate poisoning in a young child: A case report. *Oxford Medical Case Reports*, *2021*(2), 59–60.

Song, Y., Li, C., Luo, F., & Tao, Y. (2019). Clinical features and risk factors of acute kidney injury in children with acute paraquat intoxication. *Journal of International Medical Research*, *47*(9), 4194–4203.

Truebold, A., Shipp, E., Han, D., & Ross, J. (2016). Pesticide-Related Hospitalizations Among Children and Teenagers in Texas, 2004–2013. *Public Health Resports*, *131*, 588–596.

ULSETH, E. T., FREUCHEN, A., & KÖPP, U. M. S. (2022). Acute poisoning among children and adolescents in southern Norway. *Tidsskrift for Den Norske* .

Vilaça, L., Volpe, F. M., & Ladeira, R. M. (2020). Accidental poisoning in children and adolescents admitted to a referral toxicology department of a Brazilian emergency hospital. *Revista Paulista de Pediatria*, *38*.

von Fabeck, K., Boulamery, A., Glaizal, M., de Haro, L., & Simon, N. (2020). Buprenorphine poisoning in children: a 10-year-experience of Marseille Poison Center. *Fundamental and Clinical Pharmacology*, *34*(2), 265–269.

Wang, G. S., & Hoyte, C. (2019). Novel Drugs of Abuse. *Pediatrics in Review*, *40*(2), 71–78.

Warrick, B. J., Tataru, A. P., & Gerona, R. (2017). New Psychoactive Substances in Pediatric Patients. In *Pediatric Clinics of North America* (Vol. 64, Issue 6, pp. 1223–1241). W.B. Saunders.

Welch, M. J., & Correa, G. A. (1980). PCP Intoxication in Young Children and Infants. *Clinical Pharmacology*, *19*(8), 510–514.

William, H., Andrew, S., Saul, N., & Olivia, L. (2007). A Report of Two Deaths from Massive Ibuprofen Ingestion. *Journal of medical toxicology*, *3*(2), 52–55.

Winstanley, E. L., & Stover, A. N. (2019). The Impact of the Opioid Epidemic on Children and Adolescents. *Clinical Therapeutics*, *41*(9), 1655–1662.

Wong, K. U., & Baum, C. R. (2019). Acute Cannabis Toxicity. *Pediatric Emergency Care*, *35*(11), 799–804.

Woolfenden, S., Dossetor, D., & Williams, K. (2002). Children and Adolescents With Acute Alcohol Intoxication/Self-poisoning Presenting to the Emergency Department. *American Medical Association*, *156*, 345–348.

Yehya, A., Albals, D., Issa, R., & Fawadleh, A. (2020). Retrospective assessment of acute poisoning incidents by pharmaceutical agents in Jordan: Data from Pharmacy One™ Poison Call Center, 2014 to 2018—Part II. *Pharmacology Research and Perspectives*, 1–7.

Zhang, Y., Yu, B., Wang, N., & Li, T. (2018). Acute poisoning in Shenyang, China: A retrospective and descriptive study from 2012 to 2016. *BMJ Open*, *8*(8), 1–11.

Zimmerman, J. L. (2012, October). Cocaine Intoxication. *Critical Care Clinics*, *28*(4), 517–526.