

**Acute drug intoxication in childhood:
10-year retrospective observational single-centre study and case reports**

Michal Buchta, Vendula Drietomská

12/2020

Summary

Background

Medication poisoning in children is one of the severe conditions that can endanger a child's life. Although drug intoxications are easily preventable, awareness of the proper handling of drugs and their safe storage out of the reach of children is not widespread among laymen society. In this work, we examined the demographic and clinical data of children admitted to the Department of Pediatrics of the University Hospital Olomouc for acute drug-induced intoxication.

Setting

Department of Pediatrics of the University Hospital Olomouc, Czech Republic

Method

Cases of drug-induced intoxication were selected from a group of patients under the age of 19 admitted to the hospital for poisoning between January 1, 2010, and December 31, 2019. Medical records of these children were prospectively evaluated with the creation of overview tables and graphs of predefined research objectives.

Results

During the given time period, 162 cases of suspected drug intoxication in children were hospitalized in the Department of Pediatrics of the University Hospital Olomouc. Of these, 108 cases were reported in girls and 54 in boys (66,7% vs 33,3%). In 16 cases (9,9%) it was a severe intoxication requiring follow-up intensive care. There was one fatal accidental intoxication. Most poisonings were observed in toddlers age (65; 40,1%). Intoxication with suicidal ideation was observed in 44 cases (27,2%), with a higher incidence of suicidal attempts in girls (40 vs 4). Repeated intoxication was recorded in 9 cases. Analgesics were the most common drug group (61; 37,7%), with paracetamol (28; 17,3%) being the leading drug. In 154 cases (95,1%), the drugs were used orally, most often in the form of tablets.

Conclusion

Accidental drug intoxications were most frequent in the age group from one to three years old. The second highest incidence of drug intoxications was among adolescents, most of whom were suicide attempts. Analgesics and psychoactive agents were responsible for the majority of cases. The medications should be kept in places where children cannot reach them to avoid childhood poisoning that may have widespread and serious consequences.

Keywords: medication poisoning, drug intoxication, children, adolescents

Introduction

In addition to injuries, poisoning is one of the most common acute conditions threatening the health and life of children and adolescents. According to data published by the Toxicological Information Center (TIC) in Prague, most of the poisonings consulted are caused by drugs (38.8% of all poisonings) in both adults and children. The available data also show that the number of drug intoxications in the Czech Republic is increasing every year. In 2019, 11 510 cases of intoxication were recorded in children under 15 years of age, which represents 54.8% of all intoxications in a given year. Drug intoxications are most commonly observed in toddlers aged 1 to 3 years. Most intoxications at this age are accidental. Especially at such a young age, the drugs overdose can cause irreversible damage to the body and acute conditions resulting in the death of a child. Intoxication caused by a parent or other family member and caused by giving the wrong dose is characteristic of children under half a year of age (Pawlowicz et al. 2013; Sahin et al. 2011). The second most numerous age group at risk of intoxication is adolescents from 15 to 19 years. It is characterized primarily by intentional intoxication in the sense of suicide attempt (Bentur et al. 2010). Many children at this age solve problems in relationships, school or family background. In these long-term uncomfortable situations, they see suicide as a possible way out of his misfortune. Fortunately, these attempts are primarily demonstrative, and most children are intimidated by their actions and seek professional help. Drug intoxications are reversible by medical intervention and usually do not end in death. However, they can leave long-term damage to the body, especially the liver and kidneys.

As for errors and accidents associated with misadministration of prescribed drugs, the victim commonly is a very young child. Those cases can involve situations of accidental swap of medications or their inappropriate use and dosage. Another cause can be a wrong understanding of the recommended dosage; also, it is not uncommon for different family members to give separate doses independently from one another (Rakovcová 2013).

The toxic dose of a certain active substance is determined individually for a given age of the child. The concentration of the intoxicant is estimated according to the amount of tablets or other dosage form ingested. The initial estimate of the intoxicating dose is used in collaboration with TIS to determine the severity of the condition and to decide on immediate primary intervention. Quantitative toxicological examination of plasma is used to more accurate determination of the actual substance concentration in the organism. Another possibility of detecting the substance in the body is a toxicological examination of gastric contents and urine. However, these rather qualitative tests aim to only determine the presence (absence) of an ingested intoxicant in the body.

Virtually all drug groups can cause harm to a child's health if overdosed. Cardiovascular medications, especially calcium channel blockers, beta-blockers and digoxin, pose a significant risk. Other dangerous, commonly available drugs include opiates, antipsychotics, and anticonvulsants.

However, drug intoxications are most often caused by analgesics, especially paracetamol and ibuprofen. In case of suspected and proven intoxication, it is necessary to consider a possible intervention, which is governed by the time from the introduction of the substance into the body, the type of substance, pharmaceutical form, route of administration and clinical picture of the patient. The intervention is based on the elimination of the substance from the organism. For immediate elimination from the body, the substance is removed from the stomach by inducing vomiting, aspirating the stomach contents or rinsing the stomach and administering activated charcoal, or a combination of administering activated charcoal and a laxative, so-called gastrointestinal lavage. These procedures are most effective within an hour after ingestion, with fluids within 15 minutes. Exceptions are the ingestion of sustained-release dosage forms, drugs with anticholinergic effects and severe poisoning associated with gastric and intestinal atony. Secondary elimination is indicated after absorption of the drug into the circulation and tissues. These methods include forced diuresis, peritoneal dialysis, extracorporeal methods such as hemodialysis, and hemoperfusion. Forced diuresis has a questionable effect and a relatively high risk of water and ionic imbalance. Substances suitable for dialysis have small molecular weight, small distribution space and low binding to plasma proteins (e.g. salicylates, methanol, ethylene glycol, lithium, isopropanol). Hemoperfusion is suitable for substances with low water solubility and high affinity for absorbents and low affinity for plasma proteins (carbamazepine, barbiturates, theophylline). Hemofiltration removes substances with a higher molecular weight. Administration of lipid emulsions (Intralipid) is indicated in acute poisoning by cardiotoxic drugs when severe cardiac symptoms cannot be managed in any other way. The prerequisite is their fat solubility. It is used in the treatment of poisoning by some beta-blockers, calcium channel blockers, but also by some cardiotoxic antidepressants, antiepileptics, antipsychotics. In the case of a known and available antidote for a given drug class, in addition to elimination methods, it is necessary to administer this specific antidote (Gut 2005).

There are not many studies in the world literature dealing with purely drug intoxications. Most of the work is based on a larger sample of the child population, including all types of poisoning without a more detailed specification of the substances, circumstances and motive for use. Other studies, on the other hand, deal with intoxications caused only by a selected drug group, such as opioids (Gaither et al. 2016). Specific case reports of intoxications are not traceable in any available work. Therefore, we decided to analyze cases of drug intoxications in childhood, which were admitted to the Children's Clinic of the Olomouc University Hospital in the last 10 years, and to compare our results with available studies of world literature. In addition, we present several case reports that were interesting for their circumstances of poisoning, symptomatology and clinical course. Another goal of this work is to draw attention to the risks of improper storage of medicines in households. Most poisonings in children can be easily prevented by sensible parent behaviour.

Damage to the child's health, the need for hospitalization and medical interventions are thus completely gratuitous (Meyer et al. 2007).

Aim of the study

This study focuses on the evaluation of the medicational poisonings that resulted in an admission of pediatric patients in the Olomouc University Hospital in 2010 – 2019. The accidental intoxications are distinguished from suicidal attempts and the most commonly represented drugs and drug groups to which children have access to are determined. Furthermore, the demographic indicators of a given sample of the child population are evaluated.

Ethics Approval

The study was approved by Local Institutional Research Ethics Committee [No. 1236/04 S-IV].

Method

This study was considered to be a retrospective observational descriptive study. All admissions to the Department of Pediatrics (DP) of the University Hospital Olomouc, Czech Republic were screened in the electronic Hospital Information System. A cohort of patients under the age of 19 admitted to the DP for suspected drug intoxication in the period from January 1, 2010 to December 31, 2019 was selected from this system. Patients who were admitted because of intoxication by alcohol, “street” drugs, chemical compounds, poisonous plants, food or other noxious agents were excluded from the study. Cases of adverse drug reactions arising from adequate therapy were also excluded from the final cohort of patients. Medical records were studied in detail, and toxicological analysis was evaluated in each case. The study was conducted following the guidelines of the Declaration of Helsinki. All data were processed anonymously.

The collected data included: age of the pediatric patient in intoxication, sex, the substance and its formulation, application route, source of the agent, cause of poisoning, unintentional or intentional intoxication, repeated intoxication, presenting complaints and clinical symptoms on admission, the severity of the condition, therapy for the individual condition, the length of hospital stay, the need for longer hospitalization in the ICU and information on patient's condition at discharge.

The results of the toxicological analysis, including detection of toxic agents in the gastric content, blood, urine and/or, and measurements of plasma levels of the substances were evaluated. The following methods were used at the Department of Forensic Medicine and Medical Law for toxicology analysis: thin layer chromatography (TLC), fluorescence polarization immunoassay (FPIA), gas chromatography-mass spectrometry (GC-MS), gas chromatography with electron capture

detector (GC-ECD), and highperformance liquid chromatography (HPLC). Continuous data were expressed as mean \pm standard deviation, while categorical variables as frequency and percentage.

Results

Demographic data and clinical presentations

During the given ten-year period, X (X%) poisoning cases were admitted to the DP of all X pediatric patients. 162 cases (X%) of suspected drug intoxication were analyzed in our study.

Of these, 108 cases were reported in girls and 54 in boys (66,7% vs 33,3%). Most poisonings were observed in the toddlers' age group from 1 to 3 years old (65; 40%). The age group of adolescents was the second greatest representation (33; 20,4%), followed by older school children (28; 17,3%) and preschoolers (19; 11,7%). For more detail, see Table 1. The average age of the patients was 7,2 years (see Table 2). The most cases (118; 72,8%) were of accidental intoxication, in 110 ongoing through the child's own fault and in 8 treatment mistakes of the parents or another family member. Repeated intoxication was recorded in 9 cases, however, only 6 of them was included in this patient cohort. Other cases occurred outside the observed period, or their admission took place in another medical facility. In one case, there was a repeated overdose with benzodiazepine abuse.

On admission, 48,1% of children did not report any subjective complaints or show any objective symptoms. The most common manifestations of intoxication were neurological symptoms, especially of an inhibitory nature (25,9%), such as malaise, drowsiness, somnolence, bradypsychia and confusion. The second largest group of symptoms was gastrointestinal problems such as nausea, vomiting, abdominal pain and diarrhoea that were monitored in 18,5% of cases. Other uncommon symptoms included excitatory neurological manifestations, tachycardia, headache, vertigo, convulsions, unconsciousness, dyslalia, collapse, and hallucinations.

In the majority of patients (84.6%), the condition improved within three days of hospitalization. The average length of hospital stay was 2,47 days. The longest hospitalization lasted 17 days, the shortest half a day. In 16 cases (9,9%) it was a severe intoxication requiring longer follow-up intensive care. During the study period, there was only one case of fatal accidental intoxication. The main therapeutic strategy was to eliminate the substance from the body by gastric lavage and/or by administering an adsorbent in the form of a carbo medicinalis. The next step was the administration of a possible antidote, correction of fluid and mineral management and treatment of symptomatic problems. In good clinical condition, most patients were discharged to home care. 16 patients were transferred to a psychiatric ward or another catchment hospital.

The average number of drug intoxications in the last ten years is 16 cases per year. A steady trend of increasing number of drug intoxication in children can be observed this time period with a maximum

deviation in 2012 (29 cases) due to an unusual increase of suicidal attempts. A detailed graph is shown in Figure 1.

Intoxication agents

The most common drug group was analgesics, used in 37.7% of cases. Psychotropic drugs were the second most abundant group of drugs (33.3%). Paracetamol was the most common drug causing intoxication in 17.3%, followed by ibuprofen in 12.9% of cases. Other commonly used drugs included dimethindene, bromazepam, clonazepam, alprazolam, sertraline and diazepam repeated in at least 5 cases. Less recurring drugs included diclofenac, levothyroxine, zolpidem, metoprolol, citalopram, verapamil, risperidone, gentian violet, quetiapine and propafenone. In individual cases, the source of intoxication was the following drugs: salicylic acid, levocetirizine, meloxicam, folic acid, moxastine teoclate, buprenorphine, dosulepin, atropine, bisulepin, tizanidine, melperon, betaxolol, codeine, tiapride, sertraline, tramadol, zolpidem, oxazepam, escitalopram, fluoxetine, aripiprazole, carvedilol, cholecalciferol, ferric oxide, phenoxymethylpenicillin, warfarin, perindopril, indapamid, trandolapril, propafenone, thiethylperazine, dextromethorphan, clenbuterol, zinc oxide, dutasteride, oxymetazoline, telmisartan, valproate, cholecalciferol, piroxikam, pyridostigmin, venlafaxin, losartan, furosemid, amlodipin, oxykodon, spironolakton, pregabalin, omeprazol, enalapril, atenolol, fluvoxamin, ramipril, mephenoalone, baclofen, tizanidine, guaifenesin, theophyllin, nebivolol, isotretinoin, pantoprazole, dropropizine, allopurinol, ursodeoxycholic acid, trazodone, olanzapine, clozapine and sorbiferol. A detailed frequency of the most common used drugs is shown in Figure 2. See Table 3 for drugs classification according to the pharmaceutical groups.

The route of administration was almost exclusively orally (in 95,1%). Solid dosage forms (tablets and capsules) were the most represented in 83,3%. The second most frequently ingested dosage forms were liquid (18,5%), represented by oral solutions, solutions and oils for external use, eye drops and nasal drops. A transdermal therapeutic system, suppositories and ointments were reported infrequently (2,5%).

Toxicological tests were indicated in almost all patients. Gastric content, serum and urine samples were taken as a standard to determine the concentration of the drug or its metabolite in the body. When no gastric lavage was performed, only serum and urine samples were evaluated. Qualitative confirmation by TLC or GC-MS was performed in urine and gastric content. Quantitative substance value was measured in plasma. 28,4% of cases, the presence of the substance in the organism was not proven.

Intentional intoxication

Intoxication with suicidal intention was observed in 44 cases (27,2%). In 5 of these children, it was a repeated experiment. Suicide attempts were most often demonstrative as a result of a bleak problematic situation in the family, school, or relationship. These intentional intoxications were

committed to draw attention, with no real intention to harm. In several cases, it was the culmination of a depressive attack. Only a few children had serious suicide attempts when even in the subsequent psychological-psychiatric examination, they indicated a desire to die.

The highest incidence of suicide attempts was found in girls (91.1% of all suicide attempts). The mean age at suicidal intoxication was 14.3 years. The two highest peaks in the frequency of these suicidal trials were recorded, 11 trials in 2012 and 10 trials in 2019. None of these trials resulted in death. The only dosage form chosen was tablets. In 4 cases, over 50 tablets were ingested. A mixture of at least two drugs was used in half of the intentional intoxications, and a single drug in the second half (47.7% vs 52.3%). The most commonly chosen drugs were paracetamol, used in 14 cases, and ibuprofen, used in 11 cases. Other frequent drug classes were antidepressants, with sertraline as the leading agent (4 cases), and anxiolytics of which alprazolam was chosen most often. Antihistamines, cardiovascular and antipsychotic medications were also involved repeatedly. In several cases, the toxic effect was intentionally potentiated by alcohol.

Discussion

Prevalence of intoxication by drugs in the paediatric population has a rising trend. Burghardt et al. find out that there is a correlation between adult drug prescriptions and rising paediatric exposures and poisonings (Burghardt et al. 2013). Children have more opportunities to get some drugs. There are many cases of children playing with drugs they found at home. In our study, we found out that from 118 cases of accidental intoxication was 110 caused by the child self-exposure. The most vulnerable group were children under 3 years old. In these ages, children begin to be more active, more mobile and begin to discover the world around them by putting things in their mouths. Northeast Romanian study describes the highest incidence of intoxication by drugs in 2-3 years old children (Nistor et al. 2018). In other published studies we can find data about cases of medication poisonings in children where 72% were younger than five years of age (Akin et al. 2011) or in children younger than six (Ouédraogo et al. 2012). Published data from Israel describes that 82.7% of reported paediatric poison exposures were in children under 5 years old, and the most exposures occurred were at home. (Bentur et al. 2011).

The severity of intoxication often depends on the household where the child grows up. In the household of young and healthy parents, children usually do not have the opportunity to find drugs. The risk is higher in the household where chronically ill or older people with chronic diseases live. In the National Poison Data System of the American Association of Poison Control Center dominated child self-exposure to prescription products (55%) (Bond et al. 2012). Yan-Ren Lin et al. show that neurologic system agents and analgesics were the most common causes of poisoning. Anxiolytic/hypnotic drugs (lorazepam) and acetaminophen were the most frequently occurring drugs

from the former group (Yan-Ren Lin et al. 2011). In our sample of children was the most common intoxication by analgesics and antipyretics, followed by psychotropic drugs. Paracetamol and ibuprofen were the most represented drugs. These analgesics are very popular among people for their great effectiveness, minimal side effects, low price and can be bought without a prescription. As a result, these analgesics are present in all households. Parents underestimate the toxic effects of paracetamol and ibuprofen, ignore their safe storing and leave them in easily accessible places (Mund et al. 2015). All this determines the primacy of analgesics in pediatric intoxications. Increasingly used slow release drug formulations which usually contain larger amounts of the active compound can lead to the unpredictable clinical course of intoxication (Rakovcová 2013). The similar data we can find in a study from Qatar, where analgesic and antipyretic medicines, specifically paracetamol, were the most common agents ingested by children as well (Abdelrahman et al. 2015). Shao Hui Koh et al. cite analgesics/ antipyretics and antihistamines as the most common product involved in poisoning (Shao Hui Koh et al. 2018). The drugs involved in intoxication in a study from Northwest Romania were: anticonvulsants, nonsteroidal anti-inflammatories, and paracetamol (Nistor et al. 2018).

Children in young ages discover the world by their mouths, as mentioned above. Therefore, it is no surprise that the most frequent route of use is per os. It was in 95% of cases in our study. The common occurrence of per os intoxication is proved by looking at the study of Yan-Ren Lin et al. which states that all children in their study were exposed by oral route (Yan-Ran Lin et al. 2011). In a study from Singapore, it was 98% (Shao Hui Koh et al. 2018).

In our 10-year data collection, there was a clear predominance of intoxication in girls over boys. More precisely, it was 108 girls to 54 boys. These results might be quite misleading since other studies show similar numbers for both girls and boys. For example, in a study from Taiwan, there were 39 boys (44.8%) and 48 girls (55.2%) (Yan-Ran Lin et al. 2011). Our high difference between girls and boys is caused by including 40 cases of suicidal poisoning in all the 108 cases of girls' intoxications.

Girls made up the majority of suicide attempts. In our hospital, we had 44 cases of suicide attempts by ingestion of drugs. From these 44 cases, there were 40 girls and 4 boys. We can find similar data in TIC database. TIC database presents that girls have a higher incidence of suicide attempts by drug intoxication than boys. Part of girls suicides makes 77.5%. Study from Duramaz et al., shows that suicide attempts were significantly more frequent in girls. They had 11 girl's cases and only one boy from 12 suicide cases (Duramaz et al. 2015). Predomination of girls in suicidal intoxication is because girls generally use "more aesthetic" ways. Boys are looking for more drastic ways of suicide, e.g. strangulation. It is not hard for adolescents to get drugs for their suicidal attempts.

Frequently misused drugs were paracetamol and ibuprofen, which is in agreement with the study from Zakharov et al. (Zakharov et al. 2013). The reason why these two medicaments were the most common is probably because we can find them almost in every household. Adolescents can buy them in a pharmacy without prescriptions too because in European Union countries is paracetamol prescription-free in pharmacies and non-pharmacy stores (Mund et al. 2015). When we look at different study, we can find out that antidepressants or combinations of drugs medicaments are common in suicidal attempts (Akin et al. 2011). TIC describes that the most commonly abused drugs were affecting the nervous system and anti-inflammatory non-steroids (Zakharov et al. 2013). Some of our patients took only one drug, others combined. It was almost 50/50. The average age of adolescents attempting suicide was 14,26 for girls and 14.44 for boys. These findings are in agreement with a study presented by Duramaz et al. where the average age for girls was 14.2 years old. (Duramaz et al. 2015).

Children usually stayed at the hospital for 2 days. In some cases, the actual drug intoxication was not proofed which lead to keeping the children for 48 hours observation. Same data we can find in a study from New England, where 96% of patients were hospitalized for 48 hours (Even et al. 2014). The longest hospitalization took 17 days. It was a case of 2 years old boy who was intoxicated by verapamil and propafenone. This case ended with child death. Luckily, it is the only fatal case of drugs intoxication in 10 years long period in our Faculty Hospital.

Child drug poisoning is a common preventable child injury. Ways to prevent these intoxications are to use child-resistant packaging and drugs take back programs (White and Kibalama 2017). Another important part of prevention is instructing parents about proper storing and usage of medicine for children. The first issue might be solved by using of lockable first aid kits or another place outside of the children's reach since especially young children find medicine quite appealing for its colourful design and tend to play with it. For the latter case, only in our study there were 6 cases of accidental intoxication (out of 117) caused by wrong drug dosage. To avoid these accidents, parents should be properly instructed about the dangers of child overdose. Parents should be properly instructed in the dangers of child overdose. In the prevention of drug intoxication, we should also pay attention to adolescents, especially girls. Wang et al. pointed out the risk of using medication organizers which can increase the number of intoxications in children (Wang et al. 2017).

Case presentations

We present 8 case reports from our group of patients with drug intoxication interesting for their circumstances of poisoning, symptomatology and clinical course. According to the cause and motive, they are divided into three categories - accidental intoxication, suicidal attempts and intoxication of an experimental nature.

1. Accidental intoxication

Case 1

An almost 2-year-old boy was admitted for a vague impairment of consciousness caused by severe accidental intoxication. At admission, he was severely hypotensive, with an irregular and fluctuating rhythm with numerous extrasystoles. He was pale with a collapsed periphery, an intangible pulse and mydriatic pupils. He reacted with severe bradycardia during handling.

After admission to the ICU DP, gastric lavage was performed, in which no tablet residues were found. 10 g of activated carbon was administered. Oxygen therapy was started. For severe bradycardia, atropine, continuous tensamine, norepinephrine and sequentially isoprenaline were administered. Furthermore, calcium, lipid emulsion and a charge of crystalloids were applied continuously. Bicarbonate was given for signs of combined acidosis in blood tests.

Circulatory was still very unstable; mean blood pressures fluctuated in the range of 19-40 cm H₂O. Diuresis was minimal. Therefore, ongoing catecholamine therapy, in combination with dobutamine, norepinephrine and isoprenaline. Atropine was administered for persistent bradycardia. Amoxicillin was used to prevent bacterial infection.

After about two hours, convulsions developed, responding relatively well to diazepam. The boy was ventilated without problems, saturation above 94%, blood gas values were satisfactory. After another three hours, glucagon was given for hypoglycemia. In the following hours, further seizures, blood pressure fluctuations, bradycardia, ventricular tachycardia, severe hypotension and oligo- / anuria recurred. The pupils did not respond to the exposure.

Approximately 24 hours after intoxication, a toxicological examination of the serum was performed, in which verapamil was detected at an already therapeutic level. In the following days, the situation gradually stabilized. The boy was already convulsive, circulatory stabilization, ventricular tachycardia disappeared, and diuresis resumed. However, the imbalance of the internal environment persists with a tendency to hypernatremia, hyperglycemia and high serum osmolality. Plasma is given for thrombocytopenia with coagulopathy. The boy was still comatose, unresponsive to painful stimuli, pupils no longer responding to exposure. The digestion was extincted.

Seven days after intoxication, brain MRI was supplemented, post-hypoxic changes in white matter were described. An increase in CRP was noted in a control laboratory blood test. ATB therapy was changed to meropenem to detect the bacterial infection on BAL examination. The boy began to digest intermittently, diuresis was maintained by the administration of furosemide or desmopressin. However, the child's neurological condition remained unchanged. Areflexia above C1 was diagnosed. Clinical examination confirmed presumed brain death. After completing the angiography of the brain, brain death was stated. Organ procurement was performed 17 days after intoxication for donation with parental consent.

Case 2

An 11-month-old baby girl admitted for a vague impairment of consciousness. Her parents noticed that she acted drunk during the day. She was put to bed in the afternoon. Twitching of the tongue was observed during sleep. When trying to wake up, she always made only second eye contact. Her parents decided to go to the hospital with her. Even before they left, they observed a breathing disorder, its irregularity with a growl. Based on these marks, they contacted the EMS. At the arrival of EMS, the girl was already atonic, bluish, cyanotic, blood pressure 85/50, pulse 126 / min, saturation 50%. Normalization of saturation to 98% after ambuvac breathing. Persistent bradypnoea. Almost no reactions to the algic stimulus were recorded, the pupils did not respond to exposure, the bulbs were divergent. Immediate transport to ICU DP.

Upon EMS arrived, child GCS was 3. She was connected to IMV for spontaneous but inadequate ventilation. Gastric lavage was performed. A sample of gastric contents together with urine and serum was sent for toxicological examination, in which metabolites of gabapentin at therapeutic levels and toxic levels of oxycodone were detected in the organism. An antidote (naloxone) was given for this finding. Therefore, the loss of consciousness was caused by acute opioid intoxication. In addition, a laboratory examination, CT for a history of a blow to the head and X-ray examination of the heart and lungs were performed. All examinations were without signs of pathological processes. In addition to naloxone, black coal was administered, and infusion therapy was initiated.

The next day on a control X-ray development of aspiration pneumonia on the right. The girl was empirically secured with co-amoxicillin. Symptomatic therapy was continued. Thanks to the stabilized condition, the girl was uncomplicatedly extubated on the 2nd day of hospitalization. An adequate decrease in oxycodone concentration was found in the control toxicological examination of the serum.

From day 4, the girl was transferred to the standard ward for further care. Here she remained afebrile with good blood count and inflammatory markers. The girl was released to home care on the same day in good clinical condition and without breathing difficulties.

Case 3

A 15-month-old baby girl admitted for ingesting an indeterminate amount of ibuprofen and intertrigo ointment. The mother found a child playing with ointment and eating it. She was dirty all over and had a full mouth ointment. The mother found that the child's older half-sister had mixed an unspecified amount of crushed ibuprofen with the intertrigo ointment. It has not been established whether this mixture was administered intentionally to the child. During the EMS transport, the child was without complications; she did not vomit.

Gastric lavage was performed on the JIRP within one hour of ingestion. Residues of ibuprofen tablets in the gastric contents. Activated charcoal was administered, and the child was admitted for observation. The child's general condition was without alteration.

The next day the child is afebrile, slightly dysphonic and laryngeal. Control biochemical examination was normal. On the same day, the child was transferred in good condition to a standard ward for realization. The behaviour was adequate to age and situation. When crying, she was mildly dysphonic without other symptoms of a respiratory infection. Samples repeated as normal except for slightly elevated AST, monocytosis, and eosinophilia. When checking, then everything is standard. The child was dismissed into home care in good general condition.

Case 4

A 2-year-old boy transferred from the children department in Jeseník for the development of severe symptoms of atropine intoxication. During the walk, the boy found a bottle of 1% atropine eye drops and drank an indefinite amount. According to the parer, 2,9 ml of solution was missing in the vial, which corresponds to 29 mg of atropine. During the development of typical symptomatology (mydriasis, restlessness, hallucinations, dry mucous membranes) admitted to the children's ward in Jeseník. Due to the unmanageable situation, he was subsequently consulted with the DP and transferred to the JIRP.

On admission, the boy had wide, mydriatic pupils without photoreaction, dry mucous membranes, was restless, and had hallucinations, defending something invisible in empty space. Toxicological examination of urine showed high concentrations of atropine and its metabolites. The administration of benzodiazepines was recommended for sedation after consulting the Toxicology Center in Prague. Physostigmine has not been recommended as an antidote due to its significant proarrhythmogenic effect. The restlessness was suppressed by the administration of midazolam and diazepam.

The next day, the unrest completely subsided. Serious rhinitis appeared after moistening of the mucous membranes. During the day, the boy was fully fed per os. Of the previous symptoms, only mydriatic pupils persisted without photoreaction. The boy was transferred back to the catchment hospital in Jeseník for significantly improve his condition.

2. *Suicide attempts*

Case 5

An almost 17-year-old girl admitted to DP via emergency department for drug intoxication out of unrequited love. In the morning, the girl probably ate all the drugs she found at home - about 10 tbl of metamizole, 20 tbl of drotaverine, 10 tbl of ambroxol, 14 tbl of propiverine, 8 tbl of

loperamide, 15 tbl of progesterone, 30 tbl of methylphenidate, 100 tbl of ibuprofen, 100 tbl of metoprolol and 20 tbl norfloxacin.

At admission, she was bradycardic, confused, with severe dyslalia and mydriatic pupils. A metabolic acidosis was found in blood laboratory tests. Gastric lavage was performed and the sample was sent for toxicological examination. Activated charcoal and atropine for bradycardia were administered. Parenteral infusion therapy was initiated with the need for catecholamines to support hemodynamics. Sodium bicarbonate administered for persistent acidosis.

Circulation, consciousness and the internal environment gradually adjusted. Liver and kidney functions were repeatedly returned to normal in the laboratory. In a stable condition, she was transferred on the 4th day of hospitalization to a standard ward, where she was examined by a psychiatrist and a psychologist. The following day, she was released to home and outpatient psychiatric care in good clinical condition.

Case 6

A 15-year-old girl transferred from the children department in Jeseník for an uncontrollable condition during intentional intoxication with trandolapril and verapamil. The girl was transported by the EMS to the children's ward in Jeseník for repeated vomiting and diarrhoea. Three empty plates of Tarka were found near her bed. At admission, a slowed psychomotor pace was evident; she was sleepy, awakened, and responded with latency. She was hypotensive 63/30 mmHg. Gastric lavage was performed after agreement with the toxicology centre. A lipid emulsion and atropine were administered. CT of the head with a negative finding was added for the finding of the spectacle hematoma. The girl was later bradycardic with a frequency of 48/min. She was transferred to the ICU DP.

There was an irregular heartbeat on arrival with a frequency of 40 / min, AV block III. degree, hypotension 60/30 mmHg, ice periphery, prolonged capillary return, GCS was 4. Noradrenaline, dopamine, midazolam, calcium gluconicum, crystalloids were used in therapy. Hypokalaemia and hypocalcaemia were substituted, hyperglycaemia corrected by intravenous insulin. Activated carbon, lactulose and fat emulsions were administered. The presence of high levels of verapamil and trandolapril was toxicologically confirmed in both urine and gastric contents.

Irregular heartbeat with bradycardia 40/min and hypotension 100/40 continued. After the administration of glucagon, transient hyperglycaemia with massive vomiting occurred. Then the cardiac output began to decrease to 1.8 l/min with a heart rate of 39/min. Cardiac output was increased after isoprenaline administration, however, there was respiratory insufficiency with hypoxemia, exacerbation of impaired consciousness, hypercapnia of 6,5 kPa, and progression of acidosis to pH 7.21. Respiratory insufficiency could occur upon aspiration after massive vomiting. The

girl was intubated and connected to controlled ventilation. After increasing the doses of isoprenaline, Cardiac output and frequency increased, vascular resistance decreased, peripheral circulation and diuresis were restored. The girl was extubated without complications after two days of favourable development. The following days she was gradually mobilized and realized. After stabilization, the girl was transferred to a standard ward and psychiatric and psychological examinations were added. The further course of hospitalization was without complications and the girl was transferred to the care of a psychiatric hospital in Šternberk 8 days after intoxication.

3. Intoxication of an experimental nature

Case 7

A 15-year-old boy was submitted for intoxication with medications he took for better sleep. The boy could not sleep because of worries about school. He found on the internet that he should take a few tablets of alprazolam in combination with codeine to calm down and sleep better. Alprazolam, which he found at home, was after the expiration date, so he preferred to take 12 tablets for a sufficient effect. However, he definitely did not want to overdose; he checked the dosage several times on the internet to make it safe. In the morning he was very tired after waking up, but otherwise in good condition. He did not confess to taking the pills and used to go to school. The teacher then noticed that the boy did not respond adequately, had wiped speech, and had difficulty moving. So she contacted the EMS and the police, who performed tests for alcohol and drugs. Then the EMS transported him to the hospital.

At admission, the boy is slightly somnolent, dysarthric, respiratory and circulatory stable. ECG finding incomplete blockade of the right Tawar arm and prolongation of the cQT interval. Laboratory only finding of respiratory acidosis. Gastric lavage was performed, activated charcoal was administered, and infusion therapy was initiated. During the follow-up examination of the other, all symptoms improved. A psychological examination was added.

At the request of his parents, the boy was released into home care on the same day in generally good condition.

Case 8

An 8-year-old girl was taken to an observation for ingestion of 1.5 tablets of unspecified drugs. A friend brought to school a bag full of peeled tablets, which she found at her grandfather's. The girl chose two coloured tablets and tried them. The teacher who found out contacted her parents. They brought the girl to the hospital.

The girl had no difficulty in receiving. She was admitted to the standard ward for observation and continuous monitoring of vital signs. Gastric lavage was not indicated. Low levels of paracetamol and

desloratadine were found in urine and serum toxicology. The girl was cardiopulmonary compensated, afebrile, without any problems during the whole hospitalization. In a stable condition, the girl was released to home care the next day.

Conclusion

In the last 10 years, 162 children and adolescents under the age of 19 have been admitted to hospital for the acute drug intoxication. Girls accounted for a total of 67% of cases. The highest incidence of intoxications was reported in toddlers between 1 and 3 years of age and in adolescents between 15 and 19 years of age. In 72% of cases, it was accidental intoxication. This was found mainly in younger age categories. The remaining 28% of cases were suicide attempts, characteristic for older school age and adolescents. Although in most cases it was only light intoxication with mild or no symptoms, several severe life-threatening conditions were reported. Unfortunately, in one case, a toddler died.

According to our results and determination of the two most numerous age groups, we need to understand drugs from several angles. They are not just a medical device to help heal or improve health. From the point of view of small children, we must also understand medicines, especially coloured ones, as attractive-looking candies-like delicacies. For older children and adolescents, medication can be an unfortunate way out of their suffering and a means of ending life. For both of these reasons, medicines should be kept out of the reach of children and parents should educate their children about the dangers of these substances.

Acknowledgments

Study was supported by an MSMT OPVV project „Toxicology“ (CZ.02.2.69/0.0/0.0/16) and by the Palacký University internal grant IGA_LF_2019_011.

Conflicts of Interest

There is no conflict of interest.

References:

1. 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. *Bmc Pediatrics*, 15(1).
2. Akin, Y., Ağzikuru, T., Cömert, S., Atilkan, P., Erdağ, G. C., & Telatar, B. (2011). Hospitalizations for pediatric intoxication: a study from Istanbul. *The Turkish journal of pediatrics*, 53(4), 369–374.

3. Bentur, Y., Obchinnikov, N. D., Cahana, A., Kovler, N., Bloom-Krasik, A., Lavon, O., Gurevych, B., & Lurie, Y. (2010). Pediatric poisonings in Israel: National Poison Center data. *The Israel Medical Association journal : IMAJ*, 12(9), 554–559.
4. Bond, G. R., Woodward, R. W., Ho, M., Chang, Y. -J., Chou, C. -C., & Wu, H. -P. (2012). The Growing Impact of Pediatric Pharmaceutical Poisoning: aspects of legislation in selected countries. *The Journal Of Pediatrics*, 160(2), 265-270.
5. Burghardt, L. C., Ayers, J. W., Brownstein, J. S., Bronstein, A. C., Ewald, M. B., & Bourgeois, F. T. (2013). Adult Prescription Drug Use and Pediatric Medication Exposures and Poisonings. *Pediatrics*, 132(1), 18-27.
6. Duramaz, B. B., Yildirim, H. M., Kihitir, H. S., Yesilbas, O., & Sevetoglu, E. (2015). Evaluation of forensic cases admitted to pediatric intensive care unit. *Türk Pediatri Arşivi*, 50(3), 145-150.
7. Even, K. M., Armsby, C. C., & Bateman, S. T. (2014). Poisonings requiring admission to the pediatric intensive care unit: A 5-year review. *Clinical Toxicology*, 52(5), 519-524.
8. Gaither J. R., Leventhal J. M., Ryan S. A., Camenga D. R. (2016). National trends in hospitalizations for opioid poisonings among children and adolescents, 1997 to 2012. *JAMA Pediatr*, (170), 1195-1201.
9. Gut, J. (2006). Otravy v dětském věku. *Pediatric pro praxi*, 6(1), 26-28.
10. 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.
11. Lin, Y. -R., Liu, T. -H., Liu, T. -A., Chang, Y. -J., Chou, C. -C., & Wu, H. -P. (2011). Pharmaceutical Poisoning Exposure and Outcome Analysis in Children Admitted to the Pediatric Emergency Department: aspects of legislation in selected countries. *Clinical Toxicology*, 52(1), 11-17.
12. Meyer S., Eddleston M., Bailey B., Desel H., Gottschling S., Gortner L. (2007). Unintentional household poisoning in children. *Klin Padiatr*, (219), 254-270.
13. Mund, M. E., Quarcoo, D., Gyo, C., Brüggmann, D., Groneberg, D. A., & Bourgeois, F. T. (2015). Paracetamol as a toxic substance for children: aspects of legislation in selected countries. *Journal Of Occupational Medicine And Toxicology*, 10(1), 18-27.
14. Nistor, N., Frasinariu, O. E., Rugină, A., Ciomaga, I. M., Jităreanu, C., & Ștreangă, V. (2018). Epidemiological study on accidental poisonings in children from northeast romania. *Medicine*, 97(29).
15. Ouédraogo, M., Ouédraogo, M., Yéré, S., Yéré, S., & Guissou, I. P. (2013). Acute intoxications in two university hospitals in Burkina Faso. *African Health Sciences*, 12(4), 483-486.

16. Pawłowicz, U., Wasilewska A., Olański W., 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.
17. Rakovcová H., (2013). Drug poisoning in children (in Czech). *Pediatric pro praxi*, (14), 126-129.
18. Sahin, S., Carman K. B., Dinleyici E. (2011). Acute poisoning in children; data of a pediatric emergency unit. *Iran J Pediatr* (21), 479-484.
19. Wang, G. S., Hoppe, J. A., Brou, L., Heard, K. J., Groneberg, D. A., & Bourgeois, F. T. (2017). Medication organizers (pill minders) increase the risk for unintentional pediatric ingestions: aspects of legislation in selected countries. *Clinical Toxicology*, 55(8), 897-901.
20. White, N. D., Kibalama, W., Pelclova, D., Brüggmann, D., Groneberg, D. A., & Bourgeois, F. T. (2018). Prevention of Pediatric Pharmaceutical Poisonings: aspects of legislation in selected countries. *American Journal Of Lifestyle Medicine*, 12(2), 117-119.
21. Zakharov, S., Navratil, T., Pelclova, D., Brüggmann, D., Groneberg, D. A., & Bourgeois, F. T. (2013). Non-Fatal Suicidal Self-Poisonings in Children and Adolescents over a 5-Year Period (2007–2011): aspects of legislation in selected countries. *Journal Of Occupational Medicine And Toxicology*, 112(6), 425-430.

Table 1: Distribution of the patients admitted for acute drug intoxication according to the age and sex

Age group	Age	Number of patients (%)	Female(%)	Male (%)
Newborns	0 - 28 d	0 (0)	0 (0)	0 (0)
Infants	29 - 364 d	10 (6,2)	7 (6,5)	3 (5,6)
Toddlers	1 - 3 y	65 (40,1)	34 (31,5)	31 (57,4)
Preschoolers	3 - 6 y	19 (11,7)	9 (8,3)	10 (18,5)
Early school age children	6 - 11 y	7 (4,3)	5 (4,6)	2 (3,7)
Schoolchildren	11 - 15 y	28 (17,3)	23 (21,3)	5 (9,2)
Adolescents	15 - 19 y	33 (20,4)	30 (27,8)	3 (5,6)
Total	0 - 19 y	162 (100)	108 (66,7)	54 (33,3)

Table 2: Average age of children with drug intoxication

Average age	Years
Total	7,17
Female	8,62
Male	4,28
Accidental intoxication	4,43
Suicide attempts	14,36

Figure 1: Frequency of children's intoxication in individual years

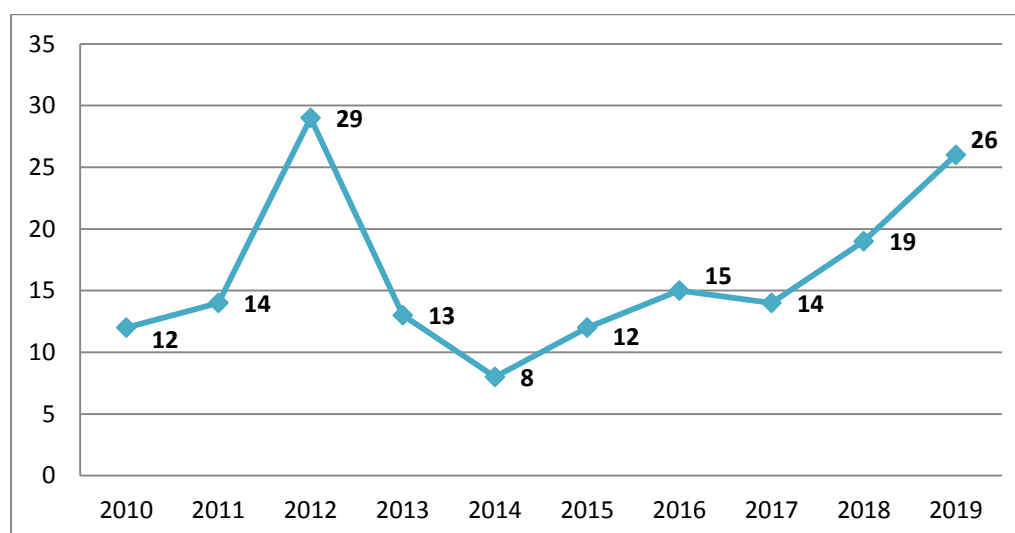


Figure 2: The most common involved drugs in children's intoxications in the study period and frequency of their use (with percentages of cases)

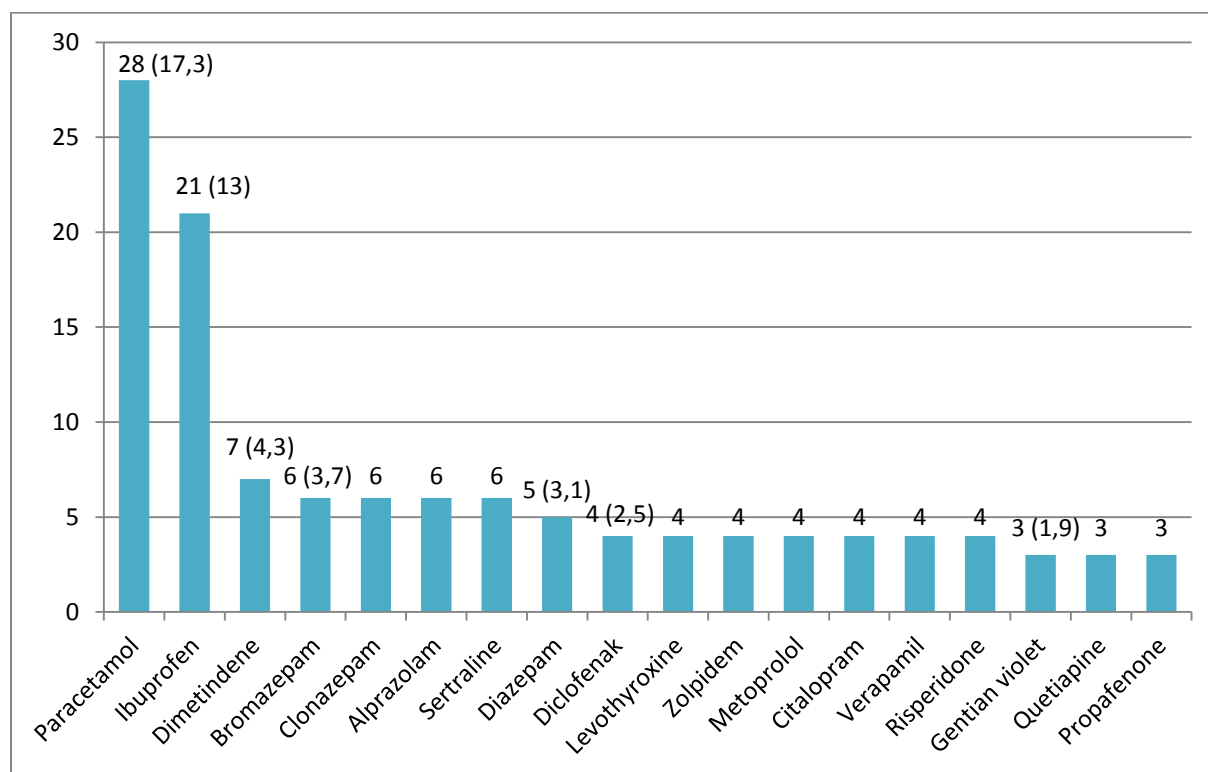


Table 3: Classification of drugs causing intoxication according to the pharmaceutical groups

Pharmaceutical groups causing intoxication	Frequency of cases
Analgesics	61
Analgesics-antipyretics	28
NSAIDs	27
Psychotropic drugs	54
Benzodiazepines	18
Antidepressants	18
Cardiotropic drugs and antihypertensives	30
Beta blockers	10
ACE inhibitors	6
Calcium channel blockers	6
Neurologic system agents	18
Antiepileptics	12
Centrally acting muscle relaxants	3
Antihistamins	12
Dermatological drugs	7
Respiratory drugs	5
Vitamins	5
Thyreotropic drugs	4
Proton pump inhibitors	3
Minerals	3
Others	18
Antiuratics	2
Antiemetics/ antivertiginosis	2
Anticoagulants	2
Unknown	2
Antibiotics	1
Prokinetics	1
Gallstones drugs	1
Venotonics	1
Alpha-1 adrenergic receptor antagonists	1
Decongestants	1
Parasympatolytics	1
Antidiabetic drugs	1
Capillary stabilizing agents	1