A Retrospective Analysis of Childhood Poisoning
Çocukluk Çağı Zehirlenmelerinin Retrospektif Analizi

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Abstract: Childhood poisonings are among the major causes of the admission to emergency units. In this study, we aimed retrospectively to determine the epidemiological and clinical characteristics of childhood poisoning among our patients. This study consisted of 1168 cases who admitted to pediatric emergency unit of our institution due to poisoning between 01/01/2011 and 14/06/2015. Poisonings were common at 13 - 48 months (44.18%). The most common poisoning agent was drugs with 545 cases (47.9%), while the second common factor was carbon monoxide poisoning with 283 cases (24.9%). Analgesic / antipyretic agents and muscle relaxants were common agents that leads to drug poisonings(127cases, 21.67%); getting multi drugs(20.3%) and mood stabilizers followed them. Among mood stabilizers, tricyclic antidepressants were the most causes of drug poisonings. 792 cases(67.8%) exposed to poisoning agent by digestion (67.8%) and 301cases (25.7%) by inhalation. Drugs appeared to be primer poisoning agents in our study. Unlike the previous studies in Turkey; poisoning by opioid analgesics and anti-neoplastic agents were also found. Although childhood poisonings are often circumvented without sequelae, they are stil major causes of admission to emergency units.
Key Words: retrospective Studies, antidepressive agents, tricyclic, child, Turkey

Kokoglu B, Bilge U, Unluoglu I, Sahin S. 2019. A Retrospective Analysis of Childhood Poisoning, *Osmangazi Journal of Medicine*, 41(2):173-181, **Doi:** 10.20515/otd.392617

Özet: Çocukluk çağı zehirlenmeleri acil servise başvuruların önemli nedenleri arasındadır. Bu çalışmada hastalarımızda görülen çocukluk çağı zehirlenmelerinin epidemiyolojik ve klinik özelliklerinin retrospektif olarak belirlenmesi amaçlandı. Bu çalışmada 01.01.2011 ile 14.06.2015 tarihleri arasında hastanemiz çocuk acil servisine zehirlenme nedeniyle getirilen 1168 olgu değerlendirildi. Zehirlenmelerin yaş gruplarına göre dağılımına bakıldığında en sık 13 ay-48 ay grubunda (%44.18) olduğu görüldü. Zehirlenme etkenlerine bakıldığı zaman en sık nedenin 545 vaka ile ilaçlar nedenli olduğu görüldü(%47.9). İkinci sırada 283 vaka sayısı (%24.9) ile karbonmonoksit zehirlenmeleriyer almaktaydı. Zehirlenmeye neden olan ilaç etkenleri arasında ilk sırada 127 vaka (%21,67) ile analjezik/antipiretik ve kas gevşeticiler; %20,3 'lük oran ile çoklu ilaç alımları ikinci sırada; duygu durum düzenleyiciler de üçüncü sırada yer almakta idi. Duygu durum düzenleyiciler arasında en çok Trisiklik antidepresanlar ile olan zehirlenme etkenlerine rastladık. Zehirlenme etkeni olan maddelerin alınış yollarına bakıldığında; 792'sinde sindirim yoluyla (%67,8), 301'inde solunum yoluyla (%25,7) alındığı bulundu. Çalışmamızda zehirlenme etkenleri olarak ilaçlar birinci sırada yer almakta idi. Daha önce ki Türkiye çalışmalarından farklı olarak; Opioid analjezikler ve anti neoplastik ajanlar ile zehirlenmelere de rastlanıldı. Çocukluk çağı zehirlenmeleri genelde sekelsiz atlatılsa bile hala acil servis başvurularında önemli bir yer tutmaktadır.
Anahtar Kelimeler: retrospektif çalışma, trisiklik antidepresan , çocuk, Türkiye

Kökoğlu B, Bilge U, Ünlüoğlu İ, Şahin S. 2019, Çocukluk Çağı Zehirlenmelerinin Retrospektif Analizi, *Osmangazi Tıp Dergisi*, 41(2):173-181, **Doi:** 10.20515/otd.392617

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Geliş Tarihi / Received 09.02.2018
Kabul Tarihi / Accepted: 24.05.2018
Online published 28.05.2018

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1. Introduction

Childhood poisoning is an important health problem that is common seen worldwide and also in Turkey. This problem may cause severe morbidity and mortality and may be a challenge for emergency units and hospitalization. In childhood poisoning, poisoning agents may differ according to neighborhood, educational status, customs and traditions and also seasons. For example, rate of poisoning by petroleum products is 42.5% in India while it's 9% in Norway. In developed countries, poisoning due to drugs are common but poisoning by pesticides and household products is higher in developing countries such as India and Thailand[1]. Therefore, each country should determine own poisoning profile and should take care of it[2]. Previous studies in Turkey have shown that most common poisoning agents were drugs(analgesics, antidepressants, antihistamines, etc), pesticides and insecticides, household chemicals, carbon monoxide, plants and foods (mushrooms, apricot seeds, etc.), respectively[3].

In childhood poisoning, presentation may be asymptomatic but may lead to a raid breakdown. Many factors including type and amount of toxic substances, formulations and efficacies of substances, exposure ways, age, weight, associated diseases, renal function, single agent poisoning or multple poisoning and onset of treatment can effect presentation of poisoning[4]. In this study, we aimed to determine poisoning risk factor in Eskisehir and to establish an approach to poisoning.

2. Methods

This study consisted of cases who admitted to Pediatric Emergency Unit of Osmangazi University Hospital, Eskisehir, Turkey between 01.01.2011 and 14.06.2015 according to the principles outlined in the Declaration of Helsinki. The study protocol and consent procedure received ethical approval *"21.07.2015; number 8"* from the Institutional Review Board of the host institution.

Patients who had food poisoning and animal bites were excluded. A total of 1207 cases who were hospitalized or monitored were detected based ICD-10 codes(X28, X29, T63, T58, T60, X44, Z71.5, Y57, T97, F10.0, X64, Z72.2), by scaning of otomated hospital records. Records of 1168 cases (in 1207 cases) were obtained in file archives, and criminal case file archives. Detailed datas of study paitents were recorded to registration forms. Demographic characteristic, admission ways, time till arrival at a hospital, type of poisoning agent, baseline biochemical parameters, clinical prognose, hospitalization-discharge status were evaluated. Results were interpreted as frequency and percentages qualitative data obtained from the study expressed as frequencies and percentages, and quantitative data were expressed as mean ± standard deviation. Statistical analyses was performed using IBM SPSS- 21.0 version. Descriptive statistics were performed.

3. Results

At 01.01.2011 - 14.06.2015 dates, totally 111834 cases admitted to Pediatric Emergency Unit(EU). 1207 of these cases 1.07% admitted to EU cause of poisoning and 1168 of them had detailed patients records. The number of boys and girls was same(584). Mean age of cases was 6.62 years (± 5.2); it was 7.38(±5.39) for girls and 5.8 years (±4.90) for boys.

Rate of poisoning cases were higher at 13-48 months(43.9%) according to distribution of poisoning based on ages (See Figure 1 for distribution of other ages).

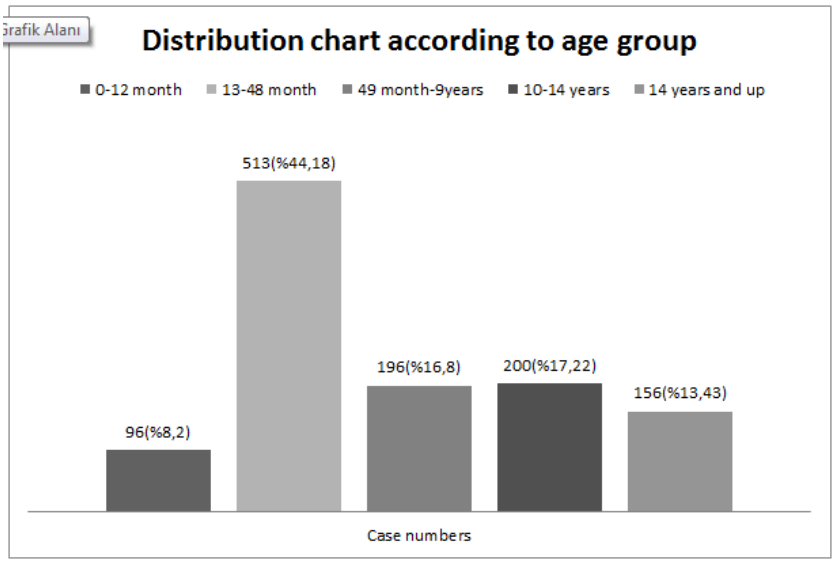

Figure 1. *Distrubution according to age group*

When we analysed distribution of poisoning based on years, most poisoning were seen in 2010 with 245. A decrease was observed between 2010-2013 but it again increased in 2014.

Analysis of poisoning agents showed that the most common agents were drugs with 545 cases(47.9%); carbon monoxide with 283 cases(24.9%) and corosive substances with 91 cases(8.01%) followed drug poisoning. Details on other poisoning agents has shown in Table 1.

Table 1.
The distribution of cases according to the poisoning agents

	Number of Cases	Percent		Number of Cases	Percent
Drugs	545	%47,9	Plants , seeds	9	%0,8
Carbon monoxide	283	%24,9	Drug + alcohol	8	%0,7
Recreational drug	91	%8,01	Mushroom	3	%0,2
Corrosive	70	%6,2	Battery	2	%0,1
Other	70	%6,2	Mercury	2	%0,1
Bleach	30	%2,7	Bleach + drug	1	%0,08
Insecticides	21	%1,8	Mushroom + drug	1	%0,08
Knowledge inaccessible				32	
Total				1136	%100
Grand Total				1168	

Exposure to poisoning agents was defined as orally, by inhalation, intramuscular and/or intravenous, transdermally and by oral+inhalation. Execpt 39 cases, all datas of 1168 patients were reached. Orally intoxication with 792 patients and inhalated poisoning with 301 patients were the most observed.

In our study, causes of poisoning were defined in 3 groups; "accidentally", "suicidal" and "iatrogenic". Rate of "accidentally poisoning" was 71.3%; rate of suicidal was 18% and the rate of cases who were iatrogenically administered wrong dose medicine (by parents or phyhicisians) were 7.6%. Repetition of suicide attempts was higher in this study; for example, we detected a case who had 5 suicide attempts.

All cases in our study were acute poisoning. Signs and symptoms at admission to EU has shown in Table 2. Most common symptoms determined as vomit. Syncope, nausea, drowsiness were other comon symptoms. Some patients(454) were asymptomatic at admission to EU. Rarely hypertension(1patient, 0.08%), pleural effusion(1patient, 0.08%), thrombocytopenia (1 patient, 0.08%) and incontinence (2 patients, 0.16%) were also reported.

111 patients of 1168 had associated chronic diseases. Suicide attempts were higher in chronic disease group compared ton on-chronic disease group and teh difference was found statistically significant ($p< 0.001$).

Table 2.
The distribution of the signs and symptoms

	Number of Cases	**Percent**		**Number of Cases**	**percent**
Vomiting	371	%31,76	Stomach ache	12	%1,02
Fainting	197	%16,86	Fever	10	%0,85
Nausea	191	%16,78	Cough	8	%0,68
Drowsiness	80	%6,84	Shake	7	%0,59
Neurological symptoms	78	%6,67	Bradycardia	7	%0,59
Headache	58	%4,96	Chest pain	6	%0,48
Convulsions	46	%3,93	Tachycardia	5	%0,42
Dizziness	29	%2,48	Skin finding	4	%0,32
Swelling of the lips	27	%2,31	Incontinence	2	%0,16
The increase in salivation	26	%2,29	Thrombocytopenia	1	%0,08
Shortness of breath	18	%1,54	Pleural effusion	1	%0,08
Eye findings	17	%1,45	Hypertension	1	%0,08
Hypotension	12	%1,02	Hypothermia	1	%0,08
Total					%100

95 patients of 1168 who were in study had substance abuse. Suicide attempts were high on substance abuse group compared ton on-abuse group. 51 patients in susbstance abuse group admitted to ER cause of suicide(53.68%). This was 5.39% in non-abuse group. There was a statistically significant difference for suicide attempt between substance abuse group and non-abuse group($p< 0.001$).

We found that causes of poisoning were drugs in 586 cases (50.1%) and non-drugs in 582 cases(49.9%).

The most common seen poisoning drugs were analgesic / antipyretic and muscle relaxants, especially paracetamol, acetylsalicylic acid, paracetamol, non-steroidal antiinflammatory drugs, opioid analgesics and muscle relaxants in 127 patients(21.67%). Rate of paracetamol

poisoning was 10.58% (62 cases) and rate of acetylsalicylic acid analgesic-antipyretic and muscle relaxants were 4,77% (28 cases).

Multi- drugs were second common causes of drug poisoning(118 cases, 20.3%).Combination of antidepressants and/or antipsychotics were often causes of multi-drug poisonings.

The other agents that cause drug poisoning were mood stabilizers(123 cases). Mood stabilizer were the causes of 20.9% of whole drug poisonings. Mood stabilizer that cause poisoning included tricyclic antidepressants (TCA), non-tricyclic antidepressants, hypnotic-sedative anxiolytics, antipsychotics, lithium and psychostimulants; but the featured one was TCA with 52 cases(8.87%). Table 3 shows details on drug subgroups.

Table 3.
Poisoning with drugs grouping according to the the active ingredient

	Number of cases	**Percent**
Antipyretic-analgesics and muscle relaxants	**127**	**%21,67**
Paracetamol	62	%10,58
Acetylsalicylic acid (ASA)	28	%4,77
ASA except Paracetamol and NSA (diclofenac, etadolak, flurbiprofen, naproxen, piracetam, dexketoprofen, metamizole sodium)	23	%3,92
Opioids	5	%0,853
Muscle relaxants	8	%1,36
Mood stabilizers	**123**	**%20,9**
Tricyclic antidepressants	52	%8,87
SSRI's	38	%6,48
Sedatives, hypnotics, anxiolytics (lorazepam, medazepam, haloperidol)	16	%2,73
Antipsychotics (paliperidone, chlorpromazine, quetiapine)	14	%2,38
Lithium	2	%0,341
Psychostimulants (methylphenidate)	1	%0,17
Cardiac Drugs	**73**	**%12,45**
Anticoagulants	28	%4,77
Beta-blockers (propranolol, nebivolol, carvedilol, metoprolol)	16	%2,73
The combination preparations	7	%1,19
Peripheral vasodilators	7	%1,19
ACE inhibitors (enalapril, lisinopril)	5	%0,853
Calcium channel blockers	3	%0,511
Alpha blockers	3	%0,511
ARB's	3	%0,511
Indapamide	1	%0,17
Hormonal drugs	**31**	**%5,29**
L-tyrosine	16	%2,73
The drosperinone + EA	7	%1,19
Levonorgestel + EA	6	%1,02
MPA,ACTH	2	%0,341
Vitamins	**23**	**%3,92**
Iron prepartions	10	%1,7
Multivitamins	9	%1,53
Vit A ,floride, zinc	4	%0,682

Antibiotics	**21**	**%3,58**
Beta laktams(penicillins, cephalosporins))	12	%2,04
Antiparasitic(metronidazole, nufroksazid, ornidazole, mebendazole)	6	%1,02
Macrolids(spiramycin, azithromycin, clarithromycin)	3	%0,511
Gastrointestinal system drugs	**17**	**%2,90**
Lansoprazole	10	%1,7
Metoklopropamid	4	%0,682
Bisacodyl, mabaver, pyridostigmine	3	%0,511
Anticonvulsants	**14**	**%2,38**
Na-valproate	8	%1,36
Phenobarbital	6	%1,02
Respiratory system	**13**	**%2,218**
Montelukast	6	%1,02
Oksolaminfosfat aminophylline, tiotropium bromide	3	%0,511
Salbutamol	2	%0,341
Theophylline	2	%0,341
Antihistamines	**8**	**%1,36**
1. *Generation (H1 receptor blockers))*	2	%0,341
2. *Generation (H2 reseptör blokörleri)*	6	%1,02
Antineoplastic	**6**	**%1,02**
The Azathioprine	3	%0,511
Methotrexate, letrozole, leflunomide	3	%0,511
Antidiyabetic	**5**	**%0,853**
Metformin	4	%0,682
Insülin	1	%0,17
Antiviral	**3**	**%0,511**
Entecavir	2	%0,341
Acyclovir	1	%0,17
Other	**3**	**%0,511**
Colchicine	2	%0,341
L-dopa	1	%0,17
Multiple Drugs	**119**	%20,3
TOTAL	**586**	%100

Analysis of treatment approaches to poisonings showed that 139 patients(11.90%) had no treatment, while 491 patients(42.03%) underwent gastric lavage and activated carbon was used for 488 patients(41.78%). See Table 4 for treatment approaches.

409 poisoned patients(35%) were discharged in EU unit, while 383 patients(32.8%) were hospitalized, 265 patients(22.7%) had intensive care, 15 patients(1.3%) had referred to another health care units. Only 1 patient has died(0.085%). 57 cases left EU and/or hospital without permission.

Table 4.
Treatment and percentages applied in the emergency department

	Number	Percent		Number	Percent
Gastric lavage/NG fitting	491	%42,03	Urine alkalisation	51	%4,36
Activated carbon	488	%41,78	Soap wash	11	%0,94
Hydration	207	%17,72	İntubation	3	%0,25
Nasal oxygen	164	%14,04	Plasmapheresis	2	%0,17
Observation	139	%11,90	Bronchodilator	1	%0,008
Hyperbaric oxygen	134	%11,64	Hemodialysis	1	%0,008
Antidote	120	%10,27	Blood transfusion	1	%0,008
Stomach Protector	67	%5,73			
MISSING DATA	38	%3,25	TOTAL	1168	%100

4. Discussion

Poisoning cases are the significant causes of admission to EU. Statistical studies on investigation of poisoning that can be critical for childhood, establishment of a management guide by analysing previous cases, observations on treatment results are important for guidance on poisonings. In this study, we determined 1207 cases(1.07) in total 111 834 admissions to EU. This rate was 2.9% in 1988, 1.8% in 1999-2001 and 2.31% in 2009. This means that admission to EU due to poisoning decreased dramatically in last 5 years [5,6,7].

On the other hand, rate of admission to EU due to poisoning is 0.28-0.66% in developped countries. Our results confirmed that poisoning is stil an important health problem in Turkey [8,9,10]

In this study, childhood poisoning has been found higher in 13-48 months children. This finding is similar to previous study repots [5,6,7, 10]. 13-48 months are oral peridos of children; a child tries to define his/her environment by taking many things to his/her mouth. This may explain frequent poisonings in 13-48 months of childhood.

In developed countries, rate of drug poisonings was about %60 in 1970s; this rate decreased to %40 by using locked cover for drug packaging [12,13,14].However this rate was 50.17% in our study. Similarly Akbay et al. found 45.2% in a previous study that was conducted in the same hospital in1999-2001 and Sahin and et al. found 48.4% in his 2009 study [5,7].

In developed countries, for a several decades drug poisoning is decreased and causes of poisoning have shifted to non-drug agents. No change has been observed in our study also in Turkey.

Carbon monoxide poisoning was the first cause of non-drug poisonings in our study (283 patients, 25%). About 5 years ago, corosive substance poisonings was more frequent than carbon monoxide poisoning. We observed that carbon monoxide poisonings increased by last 5 years. Severe weather conditions and heating systems with mechanical faulties may explain increase in poisonings due to carbon monoxide. However, all cases who admitted to ER unit due to carbon monoxide poisoning recovered without sequelae. Efficient use of hyperbaric treatment methods in Eskisehir effects

improving outcomes. Therefore hyperbaric treatment centres should be considered for cities where carbon monoxide poisonings are frequent.

In our study proportion of multi-drug poisonings to whole drug poisonings was found 20.3%. In single drug intoxication, analgesic / antipyretic medications and muscle relaxants (21.67%) constituted the largest share of drug poisonings; in this group, the most common drug was paracetamol (10.58%, 62 cases) and acetyl-salicylate followed it(4.77%, 28 cases). In our study, poisoning due to opioid analgesics has been detected in 5 cases(0.85%). Neither previous studies conducted in our hospital, nor similar studies on childhood poisoning has reported poisoning due to opioid analgesics [5,6,11,17].

The use of opioids in the pediatric age group are unsafe. Opioid poisoning may cause neurological (lethargy, agitation, stupor, convulsions, coma, respiratory depression), cardiovascular (tachycardia, hypertension) and gastrointestinal (nausea, vomiting) symptoms. Furthermore, apathy, miozis, coma, respiratory depression and convulsions due to falsely using of tramadol 100 mg suppository was reported in several cases (5 weeks and 6 months old)[18]. 5 patients with opioid poisoning in our study have been hospitalized and were discharged after an asymptomatic clinical course.

TCA's were the most common mood stabilizers that cause poisoning(8.87%); especially amitiriptilin(5.2% of all drug poisonings). This finding was paralel to other study results. As known, TCA's effect on central and peripheral nervous system and cardiac conduction system. Toxic doses of TCA's can inhibit reuptake of biological amines (serotonin and dopamine) and lead to delirium, psychosis, coma, lethargy. In addition, they have anticholinergic effects by antagonizing muscarinic acetylcholine receptors and also cause hypotension through alpha receptor antagonism. Cardiac side effects are the most cause of mortality [19,20].

SSRI's present different clinical variations between asymptomatic and death. They may lead to serotonergic syndrome associated to alterations on mental status, autonomic hyperactivity and neuromuscular anomalies. Currently, psychiatrists prefer SSRI's, but, since amitiriptilin is also preferred for rheumatic diseases such as fibromyalgia, widespread musculoskeletal pain and migraine prophylaxis, TCA's still are prescribed more than SSRIs[21,22.]

In our study, antineoplastic agents such as azathioprine, methotrexate, letrozol and leflunomide caused to poisoning in 6 cases(1.02%). There is no report on poisoning due to antineoplastic agents in previous studies conducted in our hospital(studies of Kırel et al. and Akbay et al.). Also, Ayaz et al. didn't report any antineoplastic agent in his Rize study(2008-2013). Toxicity due to antineoplastic agents depends on the clinical dose. Mucosal erosions, diarrhea, bleeding and ulcers in GIS; thrombocytopenia, leukopenia and anemia due to bone marrow suppression; bleeding disorders, mild skin lesions up to deep ulcers in the range of induration; acute renal failure; hepatotoxicity; pulmonary fibrosis may be the consequences of poisonings due to antineoplastic agents [23,24]. In our study 5 cases had exposed to antineoplastic agents accidentally, but one case(a girl,8 years old) received her mother's antineoplastic agent for suicide(we detected a second suicide attemt in her records). There was no symptom at admission exept nausea and vomit in these 6 cases. 4 cases were monitored in hospital and 2 were treated in intensive care unitbecause of alkalosis electrolyte imbalance and acidosis than they were discharged.

In this study, we observed poisoning due to opioids and antineoplastic agents. There wasn't such a finding in previous reports. Although clinical prognose of our cases were well, worse outcomes were reported in other studies. Therefore precautions should be done. Although childhood poisonings are often circumvented without sequelae, they are still major causes of admission to EU. Various works (banners, brochures, educational videos) can be organise for parents to be sensitive about hiding drugs from their childs.

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