

Evaluation of Intoxication Cases Followed up in Pediatric Intensive Care Unit During COVID-19 Pandemic with Social Restrictions

COVID-19 Pandemisi Sırasında Çocuk Yoğun Bakım Ünitesinde Sosyal Kısıtlamalarla Takip Edilen İntoksikasyon Olgularının Değerlendirilmesi

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Abstract

Introduction: Intoxication's are the preventable cause of mortality and morbidity. While most pediatric cases are asymptomatic at presentation, some patients might present with life-threatening symptoms. Patients with life-threatening symptoms need close follow-up in the pediatric intensive care unit (PICU). In this study we aim to retrospectively evaluate the demographic, epidemiologic, clinical features, and prognosis of the patients that are followed up in PICU when the social restrictions were on and to investigate the effect of these restrictions on patients with intoxication.

Materials and Methods: Patients that are followed up with intoxication between August 2020 and December 2021 when the social restrictions were on due to COVID-19 in Istanbul University of Health Sciences Turkey, Sancaktepe Şehit Prof. İlhan Varank Training and Research Hospital PICU were included.

Results: There were 50 patients with the diagnosis of intoxication that were followed up in our PICU between August 2020 - December 2021. Thirty-two of them (64%) were female and 18 of them were male (36%), and the median age was 14.9 (0.25-17.8) years. Four (8%) of our patients needed invasive mechanical ventilation support, while 5 (10%) of them needed noninvasive mechanical ventilator support. Therapeutic plasma exchange (TPE) was applied to 6 patients and charcoal hemoperfusion (CH) therapy was applied to 8 (16%) patients with various drug intoxication symptoms.

Conclusion: Life-threatening pediatric intoxication cases may be encountered. Extracorporeal therapies such as TPE and CH may be lifesaving in chosen cases. In our opinion, our study will contribute to the literature regarding the use of extracorporeal therapies without any mortal complications.

Keywords

Pediatric intensive care unit, pediatric drug intoxication, charcoal hemoperfusion

Anahtar kelimeler

Çocuk yoğun bakım ünitesi, pediatrik ilaç zehirlenmeleri, kömür hemoperfuzyonu

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Öz

Giriş: Zehirlenmeler önlenebilir mortalite ve morbidite nedenidir. Pediatrik olguların çoğu başvuru anında asemptomatik iken, bazı hastalar yaşamı tehdit eden semptomlarla başvurabilir. Hayatı tehdit eden semptomları olan hastaların çocuk yoğun bakım ünitesinde (ÇYBÜ) yakın takibi gerekir. Bu çalışmada, sosyal kısıtlamalar devam ederken ÇYBÜ’de izlenen hastaların demografik, epidemiyolojik, klinik özellikleri ve prognozlarını retrospektif olarak değerlendirmeyi ve bu kısıtlamaların intoksikasyonlu hastalar üzerindeki etkisini araştırmayı amaçladık.

Gereç ve Yöntem: Çalışmaya İstanbul Sağlık Bilimleri Üniversitesi Sancaktepe Şehit Prof. İlhan Varank Eğitim ve Araştırma Hastanesi ÇYBÜ’de COVID-19 nedeniyle sosyal kısıtlamaların devam ettiği Ağustos 2020 ile Aralık 2021 tarihleri arasında zehirlenme ile takip edilen hastalar dahil edildi.

Bulgular: Ağustos 2020 - Aralık 2021 tarihleri arasında ÇYBÜ’de zehirlenme tanısı ile takip edilen 50 hasta vardı. Hastalarımızın 32’si (%64) kadın, 18’i erkek (%36) olup, ortanca yaş 14,9 (0,25-17,8) yıl olarak saptandı. Hastalarımızın 4’ü (%8) invaziv mekanik ventilatör desteğine ihtiyaç duyarken, 5’i (%10) noninvaziv mekanik ventilatör desteğine ihtiyaç duydu. Çeşitli ilaç intoksikasyon semptomları olan 6 hastaya terapötik plazma değişimi, 8 (%16) hastaya kömür hemoperfüzyon (CH) tedavisi uygulandı.

Sonuç: Hayatı tehdit eden pediatrik zehirlenme olgularıyla karşılaşılabilir. TPE ve CH gibi ekstrakorporeal tedaviler seçilmiş olgularda hayat kurtarıcı olabilir. Çalışmamızın ekstrakorporeal tedavilerin zehirlenme olgularında mortal komplikasyonlara yol açmadan kullanılması konusunda literatüre katkı sağlayacağını düşünmekteyiz.

Introduction

Intoxication is commonly observed during childhood and it’s a preventable cause of mortality and morbidity. It is also one of the leading causes of hospitalization (1,2). Especially most of the cases before 4th age happens accidentally and better packaging technics and toxic substance awareness are significantly important for the prevention of these accidents (3). In 2020, the Annual Report of the American Association of Poison Control Centers’ National Poison Data System (NPDS) has recorded more than 2 million cases of the exposure to toxic substances, and more than 55% of these cases are acute intoxications of children under 5 years of age (4).

According to the 2018-year report by National Poison Solidarity Center, 52.5% of the intoxication cases (total number: 217.323) were below 19 of age, and 51.4% of these were children under 5 years of age (5).

While most pediatric cases are asymptomatic at presentation, some patients might present with life-threatening symptoms. Patients with life-threatening symptoms need close follow-up in the pediatric intensive care unit (PICU) (6). Although it is stated that the majority of the patients with intoxication followed-up in PICU didn’t require any major medical intervention, there is no reliable scoring system to set indications for PICU regarding acute intoxications (7). Due to this, most of the cases are internalized to PICU whether symptomatic or not.

The epidemiology of pediatric intoxications varies from country to country, and may even vary due to

regional, sociocultural, and economic specifications (8,9). Epidemiologic research is needed for preventive measures to be feasible.

World Health Organization (WHO) declared COVID-19 a pandemic on 11th March 2020, after more than 118,000 cases were observed and social restrictions were applied all over the world (10). A study from Finland between January 2017 - December 2020 has shown that lockdown and social restrictions did not reduce the incidence of heavy alcohol and drug consumption among teenagers. Even though the social restrictions have reduced the incidence of pediatric alcohol intoxications in Spring 2020, the incidence was found to be higher than past 3 years in Summer 2020 when the restrictions were lifted (11). There were no other data found regarding the intoxication cases that required pediatric intensive care during social restrictions.

In this study we aim to retrospectively evaluate the demographic, epidemiologic, clinical features, and prognosis of the patients that are hospitalized and followed up in PICU for 16 months when the social restrictions were on and to investigate the effect of these restrictions on patients with intoxication.

Materials and Methods

Patients

Patients that are followed up with intoxication between August 2020 and December 2021 when the social restrictions were on due to COVID-19 in Istanbul University of Health Sciences Turkey,

Sancaktepe Şehit Prof. İlhan Varank Training and Research Hospital PICU were included. Our PICU has 12 level three pediatric intensive care capacity. Our study is a single-centered retrospective cohort study. The patients were initially assessed at our pediatric emergency department and ones that are exposed to toxic dose of a drug, have signs of intoxication, and are advised to be followed up in PICU by National Poison Solidarity Center were internalized to our unit. Information about the patients such as gender, age, chronic disease, time and place of intoxication, arrival time to hospital, symptoms and signs, activated charcoal therapy and gastric lavage application, the poisoning severity score and treatments (mechanical ventilator support, noninvasive ventilation, hemoperfusion, plasmapheresis, renal replacement therapies, etc.) were recorded from patients' files, retrospectively. Ethics Committee Approval was given by University of Health Science Turkey, Sancaktepe Şehit Prof. İlhan Varank Training and Research Hospital Ethics Committee (Protocol Number: 13.04.2022/E-46059653-020-325). This study is carried out in accordance with the Declaration of Helsinki. Patients with missing/unreachable records and food poisoning cases except mushrooms were excluded.

Therapeutic Plasma Exchange

The therapeutic plasma Exchange (TPE) is preferred in poisoning cases with protein binding drugs when the clinical state worsens despite the conventional medical management. TPE was performed by membrane separation. Prismaflex® (Baxter, USA) TPE 1000 and TPE 2000 sets were used. The amount of plasma was calculated as "estimated plasma volume (L)=0.07 x weight (kg) x (1 - hematocrit)". Fresh frozen plasma was used as the replacement fluid. Saline 0.9% was used to prime the TPE circuit. Heparin 10-20 U/kg was administered hourly. During the TPE procedures, blood flow was adjusted to 2-6 mL/min/kg. Vital signs were thoroughly monitored during TPE procedures. Control blood samples were taken immediately before and after TPE.

Hemoperfusion

There are two major types of adsorbent materials; activated charcoal and resins. Charcoal hemoperfusion is a method that benefits from the adsorption capacity of activated carbon. Charcoal efficiently removes

molecules between the range of 1,000-1,500 kDa and has a great affinity for water-soluble molecules, whereas resins have a higher affinity for lipid-soluble molecules. Uremic metabolites, toxic substances, and creatinine easily pass through the membrane and are adsorbed from the plasma (12). In this method, blood is perfused through the Adsorba 150 and 300 (Gambro Inc., Hechingen, Germany) cartridge of charcoal granules. It is proven that these cartridges efficiently absorb the following drugs; barbiturates, organophosphates, bromocarbamide, paracetamol, ethchlorvynol, paraquat, meprobamate, phenacetin, methaqualone, and salicylate (12). In this study, hemoperfusion was performed at least for six hours according to the clinician's discretion. Blood flow was determined according to age, and heparin was used as the primary anticoagulant. Charcoal hemoperfusion (CH) therapy is preferred when the clinical state gets worse despite conventional medical management.

Statistical Analysis

Data collected were analyzed using SPSS Data Analysis version 21.0 (SPSS Inc., Chicago, IL, USA). This analysis included frequency (counts) and percentages for nominal variables, medians, and minimum-maximum values for continuous variables. Kolmogorov-Smirnov tests were used to assess the normality of the distribution of continuous variables. The alpha error was set at 0.05.

Results

There were 50 patients with the diagnosis of intoxication that were followed up in our PICU between August 2020 - December 2021. Thirty-two of them (64%) were female and 18 of them were male (36%), and the median age was 14.9 (0.25-17.8) years. The most frequent months for intoxication were March, August, and September. Forty-two (84%), 7 (14%), and 1 (2%) of the patients were exposed to toxic material at home, on the streets, and in hospitals, respectively. Among all 9 (18%) patients have a chronic disease (Table 1).

Of 50 patients 11 (22%) were symptomatic and the most frequent presentation was metabolic acidosis (n=10, 20%), followed by arrhythmia (n=6, 12%), nausea vomiting (n=5, 10%), bradycardia (n=4, 8%), stomachache (n=4, 8%), respiratory distress (n=3, 6%), tachycardia (n=3, 6%), coma (n=3, 6%), tachypnea

(n=3, 6%), mydriasis (n=2, 4%), myosis (n=1, 2%), diarrhea (n=1, 2%) and hypersalivation (n=1, 2%). Activated charcoal and gastric lavage were applied to 37 (74%) and 35 (70%) patients, respectively. According to the poisoning severity scores, 37 (74%), 3 (6%), 1 (2%) and 9 (18%) patients have scores of 0, 1, 2 and 3, respectively (Table 2). Forty-five (90%) patients had drug-related intoxications, while 2 (4%) patients had inhaled gas, 1 (2%) patients had mushrooms, 1 (2%) patient had ecstasy and 1 (2%) patient had alcohol-related intoxications. Also, 24

(48%) patients had multiple-drug intoxications. The most frequent drug was paracetamol (n=10, 20%), followed by methylphenidate (n=5, 10%), risperidone (n=4, 8%) and metformin (n=4, 8%) (Table 3).

Four (8%) of our patients needed invasive mechanical ventilation support, while 5 (10%) of them needed noninvasive mechanical ventilator support. TPE was applied to 2 patients with calcium channel blocker, 2 patients with paracetamol, 1 patient with colchicine, and 1 patient with mushroom intoxication (Table 3). Renal replacement therapies were not applied.

Features	
Gender, n (%)	
Female	32 (64)
Male	18 (36)
Age (months), median (minimum-maximum)	
	179.5 (3-214)
Month, n (%)	
January	3 (6)
February	5 (10)
March	8 (16)
April	2 (4)
May	4 (8)
June	2 (4)
July	0 (0)
August	8 (16)
September	8 (16)
October	1 (2)
November	3 (6)
December	6 (12)
Time of the day, n (%)	
08:00-16:00	17 (34)
16:00-00:00	27 (52)
00:00-08:00	6 (12)
Place, n (%)	
Home	42 (84)
Street	7 (14)
Hospital	1 (2)
The duration between exposure and application, median (minimum-maximum)	
	2 (1-72)
Underlying disease, n (%)	
Yes	9 (18)
No	41 (82)

Features	
Presence of symptoms, n (%)	
Yes	11 (22)
No	39 (78)
Type of symptoms, n (%)	
Metabolic acidosis	10 (20)
Arrhythmia	6 (12)
Vomiting	5 (10)
Bradycardia	4 (8)
Stomachache	4 (8)
Respiratory failure	3 (6)
Tachycardia	3 (6)
Coma	3 (6)
Tachypnea	3 (6)
Mydriasis	2 (4)
Myosis	1 (2)
Diarrhea	1 (2)
Hypersalivation	1 (2)
Use of activated charcoal, n (%)	
Yes	37 (74)
No	13 (26)
Gastric lavage, n (%)	
Yes	35 (70)
No	15 (30)
*Poisoning severity score, n (%)	
0	37 (74)
1	3 (6)
2	1 (2)
3	9 (18)

*A standardized scale for grading the severity of poisoning allows qualitative evaluation of morbidity caused by poisoning, better identification of actual risks, and comparability of data.

CH therapy was applied to 8 (16%) patients with various drug intoxication symptoms. Five of them were female and 3 of them were males. The median age was 162.5 months. Three patients were admitted to the PICU with calcium channel blocker intoxication, 2 patients with paracetamol intoxication, 1 patient with colchicine intoxication, 1 patient with metformin

Features	
Hospitalization duration, median (minimum-maximum)	3 (1-11)
Agent, n (%)	
Drug	45 (90)
Inhaled gas	2 (4)
Mushrooms	1 (2)
Ecstasy	1 (2)
Alcohol	1 (2)
Multidrug usage, n (%)	
Yes	24 (48)
No	26 (52)
Mostly used drugs, n (%)	
Paracetamol	10 (20)
Methylphenidate	5 (10)
Risperidone	4 (8)
Metformin	4 (8)
Mechanical ventilation, n (%)	
Yes	4 (8)
No	46 (92)
Noninvasive mechanical ventilation, n (%)	
Yes	5 (10)
No	45 (90)
Renal replacement therapy, n (%)	
Yes	0 (0)
No	50 (100)
Plasma exchange, n (%)	
Yes	6 (12)
No	44 (88)
Hemoperfusion, n (%)	
Yes	8 (16)
No	42 (84)
Use of inotropes, n (%)	
Yes	2 (4)
No	48 (96)

intoxication, and 1 patient with mushroom intoxication diagnosis. Regarding the cardiovascular symptoms, atrioventricular block was observed in 2 patients, persistent hypotension was observed in 2 patients and 2 (4%) of the patients needed inotropic support (Table 4). CH therapy was initiated due to persistent cardiovascular symptoms despite all the conventional methods. The existing symptoms were regressed dramatically in the first hour of the CH treatment. Combination of gastric lavage, activated charcoal, and N-acetyl-cysteine protocol was applied to 2 patients with paracetamol intoxications. CH treatment was initiated due to worsening clinical symptoms and laboratory findings caused by high drug concentration. All existing findings were improved after CH therapy.

Our patient with mushroom intoxication was treated with combination of gastric lavage, activated charcoal, N-acetyl-cysteine, and silybin. CH was initiated due to the worsening of clinical condition and findings were recovered after the CH therapy. None of the patients with intoxication was dead.

Discussion

Poisoning cases are common in pediatric emergencies and intensive care units. Exposure to the toxic substance might be through enteral way, by contact, inhalation, or parenteral way. Factors such as time of exposure, the biological properties of the toxic substance, the amount of intake, the removal methods for toxic substance, and the presence of antidotes are significant for the prognosis (6).

When the intoxication cases in the literature were evaluated regarding the gender and the age, the accidental intoxications were found to be more common in younger males and the suicidal intoxications were found to be more common in adolescent females (13). Although, there was no significant difference between males and females regarding the frequencies (14,15). In our study, female cases were found to be predominant (n=32, 64%). According to the study by Jung et al. (16), it is stated that poisoning cases were more common in children younger than 5 years of age, especially between 1-2 years. In a study by Gokalp (13), it is reported that the majority of the cases were male and the mean age was 51 months. In our study, the median age was 179.5 (3-214) months. In our opinion, the difference between the literature and our study is caused by the fact that the majority of our cases were suicidal.

The incidences of intoxications vary seasonally and the poisoning cases were found to be more common in spring (14), winter (16), and summer (17), according to the different studies. It is thought that the majority of the poisonings in winter and summer were due to carbon monoxide gas and suicidal intoxications, respectively. When we analyze our study in terms of date and time, we found that most of the cases were observed in March, August, and September, and most of them were applied to hospitals between the hours of 16:00-24:00. As in terms of age and gender, our data mostly represents the suicidal intoxications, rather than accidental ones.

The application time is a crucial factor for the treatment plan. The mean application time was found as 60 minutes in the study of Gokalp (13). According to many studies, most of the patients had applied to the hospital in the first hour of exposure (16). In our study,

the median application time is 2 hours (1-72), which is longer than that of in the literature. It is detected that the majority of the patients reside around our hospital. In our opinion, the delayed hospital application despite the accessible and central localization of our hospital is due to lack of knowledge and experience of the families and the suicidal nature of our cases.

The most frequent substances related to intoxications vary according to the regions and the countries. In two different studies from Romania and Brazil, the most frequent substances causing the intoxications were non-medical materials and the majority of them were chemical products that are used in the household (3,18). In a study by McGregor et al. (19), the most common substances according to the NPDS data were cosmetic products. In another study by Hassan and Siam (20), the most frequent substances were reported as pesticides. On the other hand, there

Table 4. Clinical applications of the cases treated with hemoperfusion

Cases	1	2	3	4	5	6	7	8
Age (month)	162	182	163	155	74	101	214	200
Gender	F	F	F	M	F	F	M	M
Drugs	Metformin + metoprolol	Paracetamol + multidrug	Amlodipine + valsartan	Verapamil	Verapamil	Mushroom	Colchicine	Paracetamol
Ventilation	+	+	-	-	-	-	+	-
Plasmapheresis	-	+	-	+	+	+	+	+
Inotrope need	-	-	+	+	-	-	-	-
ECG	Bradycardia	None	Prolonged QT	2 nd degree AV Block	1 st degree AV Block	None	Prolonged QT	None
*QTc 0 (msec)	466	458	485	504	481	424	500	380
*QTc 24 (msec)	460	464	443	436	446	438	450	380
*Plt 0 (x10 ⁹ /L)	243	118	252	252	386	275	215	237
*Plt 24 (x10 ⁹ /L)	151	88	59	32	48	109	171	80
NAC infusion	+	+	-	-	-	+	+	+
Lipid infusion	-	-	+	+	+	-	+	-
Insulin + Dextrose infusion	-	-	+	+	+	-	-	-
Glucagon bolus	-	-	+	+	+	-	-	-
Urine alkalization	+	-	-	-	-	-	-	-
Calcium replacement	+	+	+	+	+	-	+	-

*0 indicates the value just before hemoperfusion therapy, and 24 indicates the value 24 hours after the initiation of hemoperfusion therapy.
 F: Female, M: Male, ECG: Electrocardiography, AV Block: Atrioventricular block, QTc: Corrected QT interval, Plt: Platelet count, NAC: N-acetyl-cysteine

are studies stating that the most common substances were drugs, in accordance with our study, and the most common groups among the drugs were reported as analgesics and antipyretics (13,15). In addition to this, some other studies indicate other drug groups for the most common substance related to intoxications (21). In our study, the most common cause of poisoning was drugs (n=45, 90%) and the most common drug was found to be paracetamol (n=10, 20%), in accordance with the literature.

In pediatric intoxication cases, along with the majority of the cases being asymptomatic, some cases may present life-threatening symptoms and need intensive care (6). In a comprehensive study that includes 12, 201 intoxication patients followed up in PICU, it is stated that 70% of them didn't require any major medical intervention and there is no reliable scoring system to set indications for PICU regarding acute intoxications (7). By the literature, the majority of our cases were asymptomatic and none of them died. Contrary to this, severe clinical conditions such as metabolic acidosis, severe arrhythmia, bradycardia, and respiratory failure occurred in 11 (22%) of our patients and extracorporeal therapies were needed. Five and 8 of our patients were treated with TPE and CH, respectively. There is no sufficient evidence for the use of TPE in poisoning cases. Nevertheless, among the indications of TPE in the guidelines of the American Society for Apheresis, mushroom poisonings and overdose drug use were stated as category II and category III, respectively (22). According to the general opinion, the efficacy of TPE regarding drug removal is higher in intoxications with drugs that have a high protein-binding affinity (23). In our study, 5 and 1 of our patients were treated with TPE due to drug intoxications and mushroom poisoning, respectively. 12 total sessions were applied. Two cases with paracetamol intoxication and 1 case with mushroom poisoning developed hepatic failure signs in the clinical course. The TPE was applied for both removing the toxic substances and reversing the hepatic failure signs. All of our patients treated with TPE for intoxication were discharged without any sequela. Our results were compatible with the literature indicating the beneficial effects of TPE in intoxication cases.

There are limited studies in the literature regarding hemoperfusion therapy, which is a blood purification modality, in drug intoxication. Hemoperfusion therapy

is preferred when the clinical state worsens despite conventional medical management (24). The most common adverse reactions during hemoperfusion therapy were reported as thrombocytopenia, leucopenia, hypocalcemia, hypophosphatemia, hypoglycemia, and hypofibrinogenemia. Previously reported complications are mostly related to catheter insertion such as bleeding, pneumothorax, or hemothorax (25). In this study, hemoperfusion procedures were performed when the clinical state had deteriorated despite the conventional and antidote treatments. CH is performed in the management of all 5 patients that are treated with TPE, in order to increase drug clearance by continuous use. Thrombocytopenia occurred in all of the patients and none of them developed any other complications. One cartridge was used for each of 3 patients with calcium blood blocker intoxication, 2 cartridges for each patient with metformin and colchicine intoxication, and 1 cartridge for each of 2 patients with paracetamol intoxication that may need liver transplantation, respectively. With CH therapy, favorable outcomes were achieved and all of the symptoms recovered.

Conclusion

Intoxications are a significant cause of pediatric emergency department applications. Especially suicidal drug intake became more frequent in the recent period, due to several factors such as the increase in the number of working mothers, smaller family sizes with urbanization, and hiring of caretakers due to long hours of work of the parents. Socioeconomic level and region of inhabitancy are significant for both incidence and causes of intoxications. Various exposure might be seen in different regions and knowing the regional difference might guide the health care professionals. Although the majority of pediatric intoxication patients are asymptomatic or mildly symptomatic, life-threatening cases may be encountered. Extracorporeal therapies such as TPE and CH may be lifesaving in chosen cases. In our opinion, our study will contribute to the literature regarding the use of extracorporeal therapies without any mortal complications.

Ethics

Ethics Committee Approval: Ethics Committee Approval was given by University of Health Science

Turkey, Sancaktepe Şehit Prof. İlhan Varank Training and Research Hospital Ethics Committee (decision no: 56, date: 12.04.2022).

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