ORIGINAL ARTICLE

An Investigation of Intoxicated Patients who Underwent Hemodialysis: A-five Year Cross-sectional study

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Abstract

Background: Hemodialysis is one of the most common extracorporeal procedures that is used for treatment in some intoxicated patients. Therefore, epidemiology and prognostic factors in hemodialysis intoxicated patients were evaluated.
Methods: In this cross-sectional study, all hospitalized patients, who underwent hemodialysis admitted to the poisoning center at Taleghani Hospital, Urmia, Iran, from 2016-2020 were evaluated. The demographic data, clinical and some laboratory findings in survivor and non-survivor group were studied retrospectively and evaluated in relation to outcome of the patients. Then, the data were analyzed by descriptive and analytical statistics using SPSS v 16.
Results: In this study, 200 (158 males, 42 females) patients were evaluated. The mortality rate was 31.5% (79% males, 21% females). Toxic Alcohol (methanol, ethylene glycol) 86 (43%) and paraquat 58 (29%) were the main causes of poisoning among the patients treated with hemodialysis. Loss of consciousness 82 (41%) and Gastrointestinal discomforts (nausea, vomiting, and epigastric pain) 68 (34%) were the most signs and symptoms in patients. Statistically significant relationships (p value < 0.05) were found between the acute renal failure and causes of poisoning. Finally, 137 patients (68.5%) were discharged with full recovery and 63 cases (31.5%) were died.
Conclusion: Because extracorporeal therapies such as hemodialysis are one of the main procedures in the treatment of poisoning and there are limited studies on the prevalence of hemodialysis in poisoned patients, this study was carried out to evaluate hemodialysis in intoxicated patients whose data can be used more widely in the future. However, more studies are required to explore the prevalence of hemodialysis in poisoned patients.

Key words: Extracorporeal therapies; Hemodialysis, Poisoning, Prognosis

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INTRODUCTION

Poisoning is a common health problem all around the world. In the United States, more than 5 million people are treated for exposure to biological or chemical agents and hemodialysis is performed for 300,000 patients, annually [1, 2]. In a similar manner, poisoning is very prevalent in Iran. About, 25000 cases are intoxicated by drug and chemicals per year in Tehran out of whom 12000 are admitted in hospital and 1200 cases are transferred to intensive care unit (ICU) and at least 120 cases die [3]. There are several ways for the management of intoxicated patients, including: supportive cares, antidote therapy, gastrointestinal decontamination, and extracorporeal treatment (ECTR) [4]. ECTR include hemodialysis (HD), and peritoneal dialysis (PD), hemoperfusion (HP), Blood exchange, and plasmapheresis. ECTR is required for 0.1% of toxins [5]. Many chemicals and drugs can be removed from the body by extracorporeal method. One of the most common methods of extracorporeal treatments is hemodialysis [4]. Some conditions affect the ability of extracorporeal therapies to eliminate toxins. As a case in point, first, the toxin substances must be very diffusible from the dialysis membrane, and the toxicity must be related to the blood level of the toxin. In addition, the body's detoxification mechanisms must be insufficient (such as acute renal failure, congestive heart failure, and pneumonia) or the toxin causes significant damage to the kidneys [6]. Also, some parameters affect the ability of hemodialysis to eliminate toxins including the small molecule, low volume of distribution, low protein binding, and highly distribution from tissue to plasma [7]. Today, ECTR is used to treat intoxication with methanol, ethylene glycol, lithium, salicylate, and phenobarbital [8-12]. Hemodialysis was first used for the treatment of Aspirin in 1950 [5]. Hemodialysis can be used to correct water and electrolyte disorders as well as the treatment of refractory metabolic acidosis and acute renal failure [4]. Likewise, hemodialysis is used in the treatment of poisoning with two

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purposes: 1) to remove dialysable toxins, 2) for the treatment of poisoning induced nephrotoxicity [6]. In a study in California in 2013, hemodialysis was the most common extracorporeal procedure used to remove toxins such as salicylate and ethylene glycol poisoning [13]. Since limited studies (if any) have been conducted on the evaluation of hemodialysis in poisoned patients in Taleghani Hospital, Urmia as the poisoning center of West Azerbaijan province, in the present study the researchers decided to evaluate the hemodialysis in poisoned patients from 2016-2020.

METHODS

In this cross-sectional study, 200 hospitalized patients, who underwent hemodialysis admitted to the poisoning center at Taleghani Hospital, Urmia, Iran, from 2016-2020 were evaluated. To conduct this study, the researchers included all hospitalized intoxicated patients who underwent hemodialysis at ages of 14 years or older during the study period. The demographic, clinical and some laboratory findings in survivor and non-survivor group were studied and evaluated in relation to outcome of the patients. Also some important data such as type of toxic substance and causes of hemodialysis were evaluated. The hospital's clinical toxicologists had visited the patients and provided further information to establish the diagnosis on admission to the ED. Patients who had no complete documents and laboratory tests during admission and were discharged with personal consent were excluded from this study. No personal identification data were recorded and all information was kept strictly confidential. Approval for performing this research was issued by the ethics committee of Urmia University of Medical Sciences, Iran. (Code: IR.UMSU.REC.1398.446). The data were analyzed using SPSS version 16 specially descriptive statistics including mean and Standard Deviation (SD). The data consisted of the demographic characteristics and clinical outcomes for each patient. The variables were also grouped into survivors and non-survivors. In this study, the differences in quantitative variables with normal distributions and abnormal distributions were evaluated by the T-test and Mann–Whitney U-test, respectively. The relationships between categorical variables and the outcomes were evaluated using Chi square test where appropriate. Also, p-value <0.05 and confidence interval of 95% found to be statistically significant.

RESULTS

In this study, among 13245 hospitalized patients in poisoning ward, 200 (158 males, 42 females) patients underwent hemodialysis on admission time. Male to female ratio was 3.7. The patients' median age was 32 (min=14, max=80) years old. The mortality rate was 31.5% (79% males, 21% females). Table 1 presents the patients' demographic characteristics and clinical features. The highest prevalence of hemodialysis (89.9%) was reported in the age group of 14-30 years. About 53 (26.5%) of patients had history of drug and Alcohol abuse. Also, 55 (27.5%) of patients were rural and 145 (72.5%) of them were urban. About 125 (62.5%) of patients were married. Toxic Alcohol (methanol, ethylene glycol) 86 (43%), paraquat 58 (29%), opiate or opium (methadone, tramadol) 24 (12%), multidrug 24 (12%), methamphetamine 3 (1.5%), lithium 2 (1%), organophosphate 2 (1%) and mushroom 1 (0.5%) were the main causes of poisoning among the patients treated with hemodialysis, respectively. Also, loss of consciousness 82 (41%), nausea, vomiting, and epigastric pain 68 (34%) and respiratory failure 31 (15.5%), vertigo 5 (2.5%), weakness 5 (2.5%), chest pain 3 (1.5%), mucosal lesions and inflammation of oral cavity and pharynx 2 (1%) and seizure 2 (1%) were the most signs and symptoms in patients. The results of the blood chemistry analysis range and P value at admission are presented in Table 2.

Table 1. The effect of Some Demographic Characteristics and Clinical Features on Outcome of the Patients who Underwent Hemodialysis on Admission Time.

Characteristics	Survivor group Number (%), (n=137)	Non- survivor group Number (%), (n=63)	P value
A). Demographic			
Age (years), Median (min – max)	30 (16 – 80)	35 (14 – 79)	
14 – 30	71 (51.8%)	24 (38.1%)	
31 - 45	35 (25.5%)	20 (31.7%)	0.26 (Mann – Whitney U)
46 – 60	19 (13.9%)	14 (22.2%)	
Up to 60	12 (8.8%)	5 (7.9%)	
Duration of hospital stay (days)	4 (1 – 43)	3 (1–32)	0.39 (Mann – Whitney U)
Admission service			
Ward	71 (51.8%)	13 (20.6%)	0.001 (chi square)
ICU (Critical ill patients)	66 (48.2%)	50 (79.4%)	
Living area			
Urban	102 (74.5%)	43 (68.3%)	0.22 (chi square)
Rural	35 (25.5%)	20 (31.7%)	
Marital status			
Married	89 (65%)	36 (57.1%)	0.76 (chi square)
Single	48 (35%)	27 (42.9%)	
History of substance abuse	34 (24.8%)	19 (30.2)	0.18 (chi square)

Table 1. Continued.

Characteristics	Survivor group Number (%), (n=137)	Non- survivor group Number (%), (n=63)	P value
B). Clinical features and complications (using Chi square test)			
Level of consciousness • Alert (GCS=15/15) • 8/15 ≤GCS < 15/15 • Coma (GCS<8/15)	 85 (62.1%) 21 (15.3%) 31 (22.6%)	 24 (38.1%) 8 (12.7%) 31 (49.2%)	0.002
Nausea, vomiting, and epigastric pain Vertigo Weakness Chest pain Seizure Loss of vision	48 (35%) 4 (2.9%) 4 (2.9%) 1 (0.7%) 1 (0.7%) 1 (0.7)	22 (34.9%) 1 (1.6%) 1 (1.6%) 2 (3.2%) 1 (1.6%) 1 (1.6%)	0.20
Respiratory failure	32 (23.4%)	33 (52.4%)	0.000
Sinus bradycardia	13 (9.5%)	6 (9.5%)	0.28
Sinus tachycardia	28 (20.4%)	17 (27%)	0.19
Hypotension	13 (9.5%)	19 (30.2%)	0.001
Hypertension	9 (6.6%)	5 (7.9%)	0.46
Metabolic Acidosis	73 (53.3%)	37 (58.7%)	0.24
Acute Renal Failure	18 (13.1%)	23 (36.5%)	0.000
C). Treatment with Hemodialysis (using Mann – Whitney – U)			
The number of hemodialysis	2 (1-19)	2 (1 – 12)	0.08
Duration of hemodialysis (minute)	180 (15-600)	180 (120 – 450)	0.16
Cause of hemodialysis • Decontamination • Treatment of Acute Renal Failure	 127 (92.7%) 10 (7.3)	 51 (81%) 12 (19%)	0.013

Table 2. Effect of Some Laboratory Profiles on Outcome and P Value on Admission Time.

Quantitative variables	Survivor group (n = 137)	Non- survivor group Number (%), (n=63)	P value
A) Normal distributions (Mean±SD) and using T test.			
Serum Hco_3	17.85 ± 6.32	15.6 ± 7.06	0.147
B) Abnormal distributions (median (min – max)) and using Mann–Whitney U-test.			
Blood Urea Nitrogen (meq/l)	25 (7 – 312)	31.5 (4.6 – 186)	0.003
Creatinine (meq/l)	1 (0.6 – 20)	1.5 (0.7 – 13)	0.000
Blood Glucose (mg/dl)	108 (15 – 489)	152 (25 – 484)	0.000
Blood pH	7.31 (6.95 – 7.60)	7.26 (6.62 – 7.5)	0.003
Sodium (meq/l)	141 (86 – 154)	141 (130 – 159)	0.98
Potassium (meq/l)	3.9 (2.5 – 8.8)	4 (2.4 – 7.8)	0.98
Platelet (IU/L)	222000 (67000– 440000)	223000 (95000 – 475000)	0.67
Amount of consumption (cc)	200 (10– 2500)	250 (30 – 750)	0.07
White blood cells (mm^3)	10500 (1100-24400)	15000 (4100-37400)	0.000

Statistically significant relationships (p value < 0.05) were found between the outcome of the patients and demographic (admission service), clinical features (level of consciousness, hypotension and respiratory failure) laboratory profile (BUN, Creatinine, pH, WBC, Blood glucose, and acute renal failure) and treatment with hemodialysis (causes of hemodialysis). Moreover, statistically significant relationships (p value < 0.05) were found between the acute renal failure and causes of poisoning. On the other hand, there were not statistically significant relationships between the outcome of the patients and demographic (history of drug abuse, duration of hospital stays, amount of ingestion, living area, marital status and history of substance abuse), clinical features (nausea, vomiting and epigastric pain, vertigo, weakness,

chest pain, hypertension, seizure, loss of vision, metabolic acidosis sinus bradycardia, and tachycardia) laboratory profile (serum Hco3, Sodium, Potassium, and Platelet) and treatment with hemodialysis (the number of hemodialysis and duration of hemodialysis).

Finally, 137 patients (68.5%) were discharged with full recovery and 63 cases (31.5%) passed away.

DISCUSSION

Hemodialysis was the most common extracorporeal procedure used to remove toxins such as toxic alcohols and salicylate [13]. The most important causes of hemodialysis in this area were poisoning with toxic alcohols (toxic alcohol poisoning such as methanol and ethylene glycol (43%)) and herbicides such as paraquat (29%), which were shown in Table 2**.** Table 3 indicated a significant increase in hospitalized patients, who underwent hemodialysis in 2020 compared to previous years due to an epidemic of toxic alcohol poisoning in the first quarter of 2020 in this region. In 2016, more than 2 million cases of poisoning were reported by the US Centers for Disease Control. However, most of these cases were treated at home and did not require hospitalization. The most common poisoning in adult and children were analgesics (11.2%) and cosmetics (13.3%), respectively and about 25% of the patients were hospitalized. Of these, 2825 patients required hemodialysis and 36 patients required hemoperfusion, and finally 1977 patients died [12]. In 2019, Hassanian-Moghaddam et al collected data across the world with modified Delphi process and evaluated outbreak in patients with methanol poisoning. Based on the results of this study, it was shown that extracorporeal treatment (i.e., hemodialysis) and antidotes may be efficient and safe processes in the treatment of intoxicated patients [15]. In this study, among 13245 hospitalized patients in poisoning ward, 200 (1.5%) patients those who underwent hemodialysis on admission time. The mortality rate was 31.5% (79% male, 21% female). The mean age of patients was 32 years (range: 14 - 80). In a previous study, about 6,000 acute intoxicated patients were hospitalized over a 7-year period, and about 40 (0.6%) of them underwent hemodialysis or hemoperfusion. The low ratio of hemodialysis to the number of hospitalized patients in this article compared to our study may be related to different clinical settings, patient characteristics, type and severity of poisoning, and management modalities [16]. In a study conducted by Güngörer et al, in Turkey from 2006 to 2013, from 998 poisoned patients, 40 were treated with extracorporeal methods, of which 27 patients (75.0%)

Table 3. Distribution of Hemodialysis among the Patients

Toxic substance	Survivor group Number (%) (n=137)		Non-survivor group Number (%), (n=63)		Number (%) of ARF/Total
	Men 108 (78.8%)	Female 29 (21.2%)	Men 51 (80.9)	Female 12 (19.1%)	
Toxic Alcohols (Methanol and Ethylene glycol)	59 (43.07%)	6 (4.38%)	20 (31.7%)	1(1.59%)	12/86 (13.9%)
Paraquat	20 (14.6%)	15 (10.94%)	18 (28.6%)	5 (7.9%)	7/58 (12%)
Opiate (morphine, heroine, …)	8 (5.83%)	0	6 (9.5%)	0	7/14 (50%)
Opium (Methadone, Tramadol, …)	6 (4.38%)	2 (1.46%)	1(1.59%)	1(1.59%)	4/10 (40%)
Multidrug (Sodium valproate, phenobarbital, antipsychotics, TCA…)	11 (8.02%)	5 (3.65%)	4 (6.3%)	3 (4.8%)	7/23 (30.4%)
Methamphetamine	1 (0.73%)	1 (0.73%)	1(1.59%)	0	1/3 (33%)
Organophosphate	1 (0.73%)	0	1(1.59%)	0	1/2 (50%)
Lithium	1 (0.73%)	0	0	1(1.59%)	2/2 (100%)
Mushroom	1 (0.73%)	0	0	1 (1.59%)	0/2 (0%)

Table 4. Comparison of Mortality Rate in Survived and Non-Survived Cases from 2016 – 2020.

Date of admission	Total Admitted Patients	Total	Survivor group Number (%), (n=137)		Non-survivor group Number (%), (n=63)		Mortality rate (%) in survived and non-survived cases
			Men	Female	Men	Female	
2016	2921	28	13	4	9	2	39.2%
2017	2671	26	11	8	5	2	26.9%
2018	2810	31	17	3	8	3	35.5 %
2019	3601	32	13	4	13	2	46.9%
2020	1242	83	54	10	16	3	22.9%
Total	13245	200	108	29	51	12	31.5%

received hemodialysis and 9 patients (25.0%) underwent hemoperfusion charcoal. Among the patients undergoing hemodialysis, the mean age of patients was 40.1 ± 17.9 (range: 18-80) years and 20 patients (55.6%) were male. The lower mean age and the higher percentage of males and the lower percentage of females in this study in comparison to other studies may be associated to the differences between the two communities. In previous study, from 27 hospitalized intoxicated patients, methanol poisoning, valproic acid, fungi, lithium, ethanol, amlodipine, organic phosphorus, paracetamol were 10 (37%), 5(18.5%), 4(14.8%), 3(11.2) %, 2(7.4%), 1(3.7%), 1(3.7%) and 1(3.7%), respectively. Similar to our study, in these studies, toxic alcohol (methanol) poisoning was the most common cause of hemodialysis. Eleven patients died and 25 patients were discharged with full recovery and the death / total patient ratio was approximately 1 to 3 [17]. In a similar study conducted in 2013 in California, USA, hemodialysis was the most common extracorporeal method used to remove toxins. Similar to the present study, the most common causes of hemodialysis were salicylate and ethylene glycol poisoning [10]. Park et al, examined the effect of hemoperfusion and hemodialysis on patients with acute herbicide poisoning and identified that, age ($p = 0.013$), swallowed volume ($p < 0.001$) and hemodialysis after hemoperfusion ($P = 0.014$) were significant risk factors for mortality in patients with paraquat poisoning. According to the findings of this study, hemoperfusion and hemodialysis are effective and safe treatments in patients with acute herbicide poisoning. In line with the study of Park et al, in the current study, 29% of patients who underwent hemodialysis had herbicide (paraquat) poisoning [13]. Also, similar to this study, acute renal failure due to organophosphate poisoning was observed in 1% of patients [18].

LIMITATIONS

The main limitation of this study was incomplete recording of some laboratory data.

CONCLUSION

Hemodialysis or other extracorporeal therapies are an essential part of the treatment of poisoning. Although a limited number of intoxicated patients require hemodialysis, these treatments are very effective. Our study in this region showed that toxic alcohols, herbicides, and drug poisoning are the most common causes of hemodialysis. Since there are limited studies on the prevalence of hemodialysis in poisoned patients and hemodialysis and other extracorporeal procedures are invasive and costly methods in the treatment of poisoning, further studies are recommended in the future to evaluate the frequency and the risk - benefits of hemodialysis in toxic patients.

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Compliance with Ethical Guidelines

The Ethics Committee of Urmia University of Medical Sciences approved this study (Code: IR.UMSU.REC.1398.446).

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Author's Contributions

Conceptualization [Mohammad Majidi]; Methodology [Mohammad Majidi]; Investigation [Arsalan Yousefpour, Mojhdeh Mehrno]; Writing – original draft [Mohammad Delirrad]; Writing – review & editing [all authors]; Funding acquisition [all authors]; Resources [all authors]; Supervision [Mohammad Majidi].

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