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Neurological Sequels and Their Causes in Patients Hospitalized in the Toxicology Intensive Care Unit of Bahraloo Hospital, Tehran, Iran

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Background: The occurrence of neurologic complications in the intensive care units (ICUs) is one of the major risks in management of patients. These sequels may be caused by structural or metabolic disorders. The same phenomenon can be seen in the toxicology ICUs, although the toxicological effects of drugs and poisons may also cause the neurological complications.
Objectives: This study aimed to determine the frequency of neurological sequels and their causes in patients hospitalized in the toxicology ICUs.
Patients and Methods: In this descriptive study, the data of patients admitted in toxicology ICU of Baharloo Hospital, Tehran, Iran, were investigated during a 2-year period (2010 – 2011) and the patients with neurological sequels, based on neurological examination or brain computed tomography (CT) scan findings, were included. Data recorded in questionnaires were analyzed by means of SPSS software, with a significance level at $P < 0.05$.
Results: Out of 1571 patients admitted in toxicology ICU during this period, 56 patients (3.56%), with the mean ± SD age of 36 ± 13.01 years, were included. The most common finding in neurological examination was the Babinski sign (67.9%). Ischemic encephalopathy with brain edema was the most common finding on the brain CT scans of these patients (33.9%). The mortality rate was 58.9% (33 out of 56). Thirteen patients (23.2%) were discharged with vegetative state. The most common cause of neurological sequel, in this study, was hypoxia (64.3%)
Conclusions: This study, for the first time in Iran, investigated the frequency and cause of neurological sequels in toxicology ICUs. The findings can improve the prophylaxis and diagnostic programs for the patients in this field.

Keywords: Sequels; Tomography; Hypoxia; Intensive Care Units; Toxicology

1. Background

In recent years, with advances in remedial and protective measures in many acute pharmaceutical poisoning and their consequences, secondary neurologic complications to the primary disease caused by its intensity are increased. Previous studies suggest the incidence of nerve and brain death in about one third of patients admitted to the internal and surgical intensive care units (ICUs). Mortality in the presence of neurological sequel, in patients hospitalized in ICU is estimated at about 55% (compared with 29% mortality, in the absence of neurological sequel). The incidence of neurological sequel leads to a two-fold increase in the duration of hospitalization in ICU, disability and the need for ventilator and the duration of the device attachment (1). The 3 – 12% overall incidence of neurological complications in a medical ICU has been reported, which include metabolic encephalopathy, seizures, hypoxic-ischemic encephalopathy, stroke, etc. (2).

One of the major complications is coma, which can be divided into two categories: 1) Structural coma, which is often observed with focal neurologic symptoms, with evidence of increased intracranial pressure (ICP). 2) Metabolic coma, with two types of reversible and non-reversible encephalopathy, which both lack focal neurological and increased ICP symptoms. Acute stroke is observed in approximately 1 – 4% of patients admitted to the ICU without neurological problems. Acute ischemic strokes may be prevented by measures taken in the medical ICU, such as angiographic studies, the prevention of flocculation in arteriovenous shunt for dialysis, vascular interventions, air embolism, cardioversion, anticoagulation or thrombolytic therapy (3, 4). Embolism and bleeding into the brain parenchyma occur as medical or iatrogenic complications in the medical ICU (5, 6). Myoclonic jerks are common with metabolic disorders, drug consumption and hypoxia cases (1). Encephalopathy is one of the major neurological complications common in the medical ICU.

Pharmaceutical encephalopathies are common causes of consciousness loss in the medical ICU, because of the

decrease in the clearance of metabolites due to the underlying kidney and liver failure (7). Toxicology ICUs are not excluded, as a part of the medical ICU. Besides, the effects of poisoning with drugs on the central nervous system (1) and the association of neurological complications in poisoning with several drugs and toxins must be considered in the toxicology ICU (8-11). Presently, the ICU of Baharloo Hospital, Tehran, Iran, annually holds a number of cases of poisoning, as one of the active centers in Tehran, in which the evaluation of sequels and neurologic complications, in addition to defining the common cases in the sequels, can be helpful to design preventive or further diagnostic measures to examine the patients hospitalized in this section, to prevent the neurologic sequel, and also, contribute to the evaluation of neurologic sequels, with the most common poisoning cases in this section.

2. Objectives

The present study is designed to assess the prevalence of brain sequels in the patients hospitalized in the poisoning ICU of Baharloo Hospital, Tehran, Iran.

3. Patients and Methods

In this cross-sectional study, the population sample consisted of all patients admitted to the poisoning ICU of Baharloo Hospital, Tehran, Iran, who were diagnosed with neurological sequel, based on the results of medical examination and paraclinic measurements [computed tomography (CT) scan or magnetic resonance imaging (MRI)]. Demographic data and the abundance and causes of sequels were prepared, based on the examination and information in hospital records and history taken from the patients' families questionnaires. This information included age, sex, and duration of stay in the ICU, the type of poisoning, drug use and referral intervals, and the underlying disease. In this study, after recording the demographic characteristics, all samples were studied for complications, such as the loss of consciousness, respiratory complications, hemodynamic disorders, heart rhythm disorders, etc., and also, for the cause of sequel. The inclusion criteria were as follows: The presence of focal neurological signs in early examination (including fasciculation, paralysis, numbness and Babinski sign), the presence of clear disturbance in early brain CT scan; the incidence of obvious neurological complications during the hospitalization. Patients with a confirmed history of neurologic disease or hospitalized in the toxicology ICU, due to reasons other than an acute toxicity, were excluded.

4. Results

From the total 1571 patients hospitalized, only 56 patients were eligible for inclusion, of which 48 (85.7%) were males and eight (14.3%) women. The incidence of brain sequel was 5.2%, in males, and 26.1%, in women. Based on history taken, the most common cause of poisoning was opioids (methadone, morphine and heroin). The most common poisoning source in men was methadone [14 cases (29.2%)], and phenobarbital and tramadol, in women (two cases (25%) for each one). In any of the poisoning types, there was no significant difference in mean age between males and females. Urine screening test results were negative in seven patients (12.5%) (Table 1). The history of addiction was positive in 34 patients (60.7%). The most common substance abuse in these patients was represented by narcotics (Table 2).

Based on history taking, antecedents of depression (n = 7, 12.5%), hypertension (n = 5, 8.9%), seizures (n = 5, 8.9%), hepatitis (n = 4, 7.1%), chronic obstructive pulmonary disease (n = 3, 5.4%) and myocardial infarction (n = 1, 1.8%) were observed in patients. A number of 31 patients (55.4%) did not mention any previous history of physical or mental illness. None of the patients had history of head trauma. During the period of stay in the ICU, 31 patients (55.4%) presented seizures, of which the most common form of seizure were generalized tonic clonic seizure (n = 27, 84.37%). This seizure occurred with the highest frequency in five patients with amphetamines poisoning (71.4%) and five patients with methadone poisoning (35.7%). No statistically significant correlation was observed between the type of seizure and medications, or toxin consumed. On the other hand, all patients with organophosphate, diphenoxylate, glibenclamide and propranolol poisonings had an episode of seizure during the time in ICU. No statistically significant correlation was observed between the incidence of seizure and medications or toxin consumed.

Focal neurological findings at time of admission were present in 50 patients (89.3%) (Table 3). The results of the brain CT scans performed for all patients are shown in Table 4. A statistically significant correlation was found between the findings of brain CT scan with generated neurologic sequel ($P = 0.01$).

The type and frequency of the complications of neurological sequels are shown in Table 5. Statistical analysis showed a statistically significant correlation between the drug type or toxin consumed and brain sequel ($P < 0.001$), tracheostomy and neurological sequel ($P = 0.001$) and the cause of sequel and neurological sequel ($P < 0.001$).

Among the 56 patients studied, 23 (41.1%) were discharged from hospital after a period of treatment. Of these, 18 (78.26%) had a permanent tracheostomy at discharge time. Totally, 33 patients (59.9%) died due to cerebral complications, caused by poisoning. The total number of deaths in the study was 143 patients, in the toxicology ICU. The hypoxia was the most common cause of neurological sequel in patients studied (n = 36, 64.3%). Neurologic complications were observed in six patients (10.7%), caused by the direct effect of drug or poison toxicity. In the other patients (n = 14, 25%), the role of hypoxia and poisoning effects on neurologic complications were conjoined.

A significant correlation between the time delay between the drug or poison consumption and the arrival of the patient to the emergency was found ($P = 0.1$). Graph 1 was per-

formed for 13 dialysis patients. No statistically significant correlation was found between the type of poisoning and dialysis (P = 0.01). The analysis of qualitative data, based on Pearson chi-square test, and the analysis of quantitative data, based on ANOVA showed no statistically significant correlation between the neurological findings and variables. The comparison of the drugs or toxins with outcomes (discharge or death), did not show any statistically significant correlation, as depicted in Table 6. No statistically significant correlation was found between the results of brain CT scan the neurological sequel (Table 7). Comparing the neurological examination with the neurological sequel showed a statistically significant correlation (P < 0.001) (Table 8).

Table 1. The Frequency and Percentage of Urine Screening Test Results in the Subjects [a, b]

Urine Screening Test Results	Values
Methadone	13 (23.2)
Morphine	9 (16.1)
Amphetamines	9 (16.1)
Tramadol	6 (10.7)
Tricyclic antidepressants	5 (8.9)
Morphine and amphetamines	4 (7.1)
Barbiturates	3 (5.4)
Negative	7 (12.5)

[a] (n = 56).
[b] Data are presented as No. (%).

Table 2. The Frequency and Percentage of the Status of Addiction in the Subjects [a, b]

Addiction	Values
Opioids	11 (19.6)
Methadone	6 (10.7)
Amphetamines	5 (8.9)
Amphetamine + opioids	5 (8.9)
Crack	4 (7.1)
Crack + amphetamines	2 (3.6)
Tramadol	1 (1.8)
Negative	22 (39.3)

[a] (n = 56).
[b] Data are presented as No. (%).

Table 3. Focal Neurologic Findings in the Patients in the Toxicology Intensive Care Unit [a]

Neurological Finding at Time of Admission	Values
Babinski	38 (67.9)
Quadriplegia	4 (7.1)
Fasciculation	4 (7.1)
Paraparesis	2 (3.6)
Hemiparesis	1 (1.8)
Hemiplegia	1 (1.8)

[a] Data are presented as No. (%).

Table 4. The Frequency of Neurological Findings by CT Scan [a]

Neurological Findings	Values
Ischemic encephalopathy + edema	19 (33.9)
Brain edema	12 (21.4)
Cerebral infarction	10 (17.9)
Herniation + edema	3 (5.4)
Bleeding	2 (3.6)
Necrosis of basal ganglia	1 (1.8)
Ventricular bleeding	1 (1.8)
Normal CT	7 (12.5)

[a] Data are presented as No. (%).

Table 5. The Type and Frequency of Neurological Sequel Observed [a]

Type of Complication	Values
Vegetative status	13 (23.2)
Spasticity of four organs	5 (8.9)
Blindness	2 (3.6)
Hemiplegia	1 (1.8)
Hemiplegia + tremor	1 (1.8)

[a] Data are presented as No. (%).

Table 6. The Comparison of Toxicity, Based on Drug or Poison Consumed [a, b]

Poisoning Type	No. of Cases	Consequence	
		Discharge	Death (33 People)
Methadone	14	6 (26.1)	8 (24.2)
Morphine	8	2 (8.7)	6 (18.2)
Heroin	2	0	2 (6.1)
Some medications	4	3 (13)	1 (3)
Phenobarbital	4	0	4 (12.1)
Propranolol	1	1 (4.3)	0
Glibenclamide	1	1 (4.3)	0
Diphenoxylate	1	0	1 (3)
Amphetamines	7	3 (13)	4 (12.1)
Tramadol	6	2 (8.75)	4 (12.1)
Methanol	3	2 (8.75)	1 (3)
Carbon monoxide	2	2 (8.75)	0
Hydrogen sulfide	1	0	1 (3)
Opioids	2	1 (4.3)	1 (3)

[a] (P = 0.3), the percentages are based on the consequence.
[b] Data are presented as No. (%).

Table 7. The Comparison of the Findings of Brain CT Scan With Residual Neurological Sequel [a, b]

Brain CT Scan Result	No. of Cases	Neurological Sequel					
		Death	Vegetative State	Spasticity of Four Organs	Blindness	Hemiplegia	Hemiplegia + Tremor
Ischemic encephalopathy + brain edema	19	10 (52.6)	6 (31.6)	2 (10.5)	0	0	1 (5.3)
Brain edema alone	12	10 (83.3)	0	2 (16.7)	0	0	0
Infarct + brain edema	10	6 (60)	3 (30)	0	0	1 (10)	0
Natural	7	2 (28.6)	2 (28.6)	1 (14.3)	2 (28.6)	0	0
Brain edema + herniation	3	1 (33.35)	3 (66.7)	0	0	0	0
Intracranial hypertension	2	1 (50)	0	0	0	0	0
Intraventricular hemorrhage	1	1 (100)	0	0	0	0	0
Bilateral necrosis of the basal ganglia	1	1 (100)	0	0	0	0	0
Not performed	1	1 (100)	0	0	0	0	0

[a] (P = 0.09), the percentages listed are based on brain CT scan results.
[b] Data are presented as No. (%).

Table 8. Comparison of the Neurologic Findings at the Time of Admission With Residual Neurologic Sequel [a, b]

Initial Neurological Examination	No.	Neurological Sequel					
		Death	Vegetative State	Spasticity of Four Organs	Blindness	Hemiplegia	Hemiplegia + Tremor
Babinski	38	26 (68.4)	10 (26.3)	2 (5.3)	0	0	0
Asymptomatic	6	3 (50)	0	1 (16.7)	2 (33.3)	0	0
Fasciculation	4	2 (50)	0	1 (25)	0	0	1 (25)
Paraparesis	2	0	1 (50)	0	0	1 (50)	0
Hemiplegia	1	1 (100)	0	0	0	0	0

[a] (P < 0.001), the percentages mentioned are based on the initial neurological examination.
[b] Data are presented as No (%).

5. Discussion

The incidence of neurological sequel due to the effect of acute drug poisoning was observed in one third of patients admitted to the internal and surgical ICUs (1). Mortality due to the cerebral complications is greater than the mortality of the same patients, without the complications. To date, a small number of researches have been conducted in this regard. This study is performed in the ICU of Baharloo Hospital, Tehran, Iran, over a period of 2 years, given the importance of the study of neurological sequels in mortality and its effect on increasing the duration of hospitalization in the ICU and the need for ventilation. The results showed that 56.3% of the patients have focal neurological symptoms or an abnormal CT scan that incurred the neurological sequel and complications caused by acute toxicity. A proportion of 23.7% of deaths were due to cerebral reasons. The frequency of neurological sequels in internal ICU was increased in previous reports, compared to our findings. Considering the wide range of internal diseases and their neurological complications, this difference is justifiable (1, 2).

Meanwhile, the death rate from neurological sequel in our study is similar to previous findings in ICU, indicating the importance of the neurological sequel (1).

The common neurological sequel in the discharged patients was the vegetative state. The most common of the radiographic findings in the patients was ischemic encephalopathy, with cerebral edema. The most common cause of vegetative state was head injuries, although cardiorespiratory arrest caused by heart disease or metabolic (e.g. hypoglycemia) is also involved in the creation of neurological sequel (12). Pathologic imaging was mainly visible in sub-cortical white matter, although it is possible that no pathological findings be clearly visible in the brain (13). Other neurological sequels observed in this study included spasticity of four organs, blindness, hemiplegia and hemiplegia with tremor. Previous studies on

the occurrence of tremor and myoclonic jerks focus on metabolic diseases and drug consumption (14). In our study, 78.26% of patients had a permanent tracheostomy on discharge. Our survey showed that 85.7% of patients were male. This indicates that more men than women use drugs, as a suicidal factor. Methadone poisoning was the most common cause of poisoning (25%).

The most common finding in the neurological examination on the admission time and the brain CT scan of patients with methadone poisoning was the Babinski sign (71.42%) and cerebral edema alone (35.71%), respectively, with the mortality rate of 57.14%, and all poisonings with heroin, phenobarbital and hydrogen sulfide were eventually lethal. According to the studies performed in medical ICU, all types of seizures were hospitalized in less than 5% of patients (2). The incidence of seizure in all patients in toxicology ICU was 2.03%.

This study aimed, for the first time, to investigate the prevalence and causes of neurological sequels in toxicology ICU. The findings of our study, conducted in the toxicology ICU of Baharloo Hospital as one of the two major university centers for the admissions of drug-poisoned patients in Tehran, showed that the incidence of neurological complications in the patients admitted to the department within 2 years was 3.56%. The most common cause of neurological sequel in this study was hypoxia. The interval between the tablet consumption and the arrival of patient to the emergency department indicates the maximum delay in the patients who eventually suffered from permanent neurological sequel or were deceased due to the complications of hypoxia. Accordingly, rapid referral to specialized treatment centers for poisoned patients can result in a significant decrease in the incidence of neurological complications and sequels in the patients.

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