Original Article

Clinical Profile of Patients with Baclofen Poisoning in an Academic Medical Center

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Abstract

Context: Baclofen overdose acutely affects the nervous system and induces a decrease in the consciousness level, coma, and death. The diagnosis of it is based on the patient's history and clinical findings. **Aims:** The present study aims to investigate baclofen-induced poisoning based on medical reports in a 5-year period. **Materials and Methods:** This retrospective study was conducted in Loghman Hakim Hospital, Tehran, Iran. The medical profile of 135 patients with baclofen overdose was read out, collected, and analyzed using SPSS version 18. **Results:** The average age of 135 patients was 26.37±18.73 years. The majority of them were female (68.1%) and intentional attempts (66.7%). There were 117 patients (86.7%) with central nervous system symptoms. The most common nervous finding was drowsiness (n = 53, 45.3%). There was no patient with seizures. There was a significant statistical relationship between the dose of baclofen and consciousness level (GCS ≤12: 302.61 ± 236.40 mg, and GCS >12: 162.21 ± 121.02 mg, $P < 0.001$). **Conclusion:** Baclofen overdose should be considered in patients referred to the emergency department with drowsiness symptoms and decreased consciousness level. Because of this poisoning, it has no specific symptoms and is common in female and young people.

Keywords: *Baclofen overdose, baclofen poisoning, clinical findings, severity*

Introduction

Baclofen is a selective agonist of the gamma-aminobutyric acid (GABA) B receptor, which is a metabotropic receptor and may reduce dopamine release and N-methyl-D-aspartate transmission.[1] Baclofen is used to treat muscle spasms in some neurologic diseases such as multiple sclerosis, spinal cord injury, and cerebral palsy.[2,3] This drug is also prescribed in patients with alcohol dependency to decrease consumption.[4] Baclofen is absorbed from the gastrointestinal tract and removed by the kidney after partial liver metabolization.[3] The half-life of it is almost between 4.5 and 6.8 h, which increases in renal failure patients.[5] Baclofen overdose can occur in intentional or accidental ingestion that affects the central nervous system (CNS), leading to respiratory depression, coma, hypotonia, drowsiness, cardiac complications (heart block, heart dysfunction, hypotension, and bradycardia), and seizures. Baclofen overdose is curable with timely diagnosis and treatment. Treatment of this poisoning is supportive care for 72 h, and in patients affected, the renal disease will likely be longer.[6,7] Baclofen poisoning has been reported in some cases with various clinical manifestations, even with an anoxic encephalopathy.[6,8-10] Based on our knowledge, there was limited evidence from clinical profile of the patients with baclofen poisoning. However, this study is a medical report from the patients with baclofen overdose in a 5-year period.

Materials and Methods

This retrospective observational study was conducted in Loghman Hakim Hospital (Tehran, Iran). The present study investigated 135 patients with baclofen overdose who were admitted to the poisoning center of the hospital from 2011 to 2016. The baclofen ingestion of them was confirmed by emergency report, family, or friend(s). Inclusion criteria were male or female patients with all ages and medical histories, and exclusion criteria were coincident usage of medicines. The researchers extracted data (demographical and clinical characteristics) from the medical records of the patients. Gathered data consisted of age, sex, cause of ingestion, clinical manifestations and outcome, Glasgow coma score (GCS) at the time of hospital admission, and biochemical tests. Also some cases had required doing intubation and mechanical ventilation. The

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dose of ingested baclofen was determined based on patients' self-reports recorded in the medical profile. In order to grade the severity of poisoning, a poison severity score (PSS) was used. The PSS is a classification of acute poisoning, regardless of the type of agents based on symptoms or signs of poisoning. It includes clinical findings of various organs such as cardiovascular, nervous system, muscular system, respiratory system, gastrointestinal tract, metabolic, blood, kidney, and liver functions. The existence of a particular symptom or sign from each organ is checked based on the PSS scheme, and then the most severe findings (symptoms or signs) were considered the severity grade.[11] The PSS has five classes that include 0 to 4. NONE (PSS 0): no symptoms or signs related to poisoning, (PSS 1): mild, transient, and spontaneously resolving symptoms, (PSS 2): pronounced or prolonged symptoms, (PSS 3): severe or life-threatening symptoms, and (PSS 4): death[11,12] [Table 1].

The patients were divided into two groups based on GCS due to the nervous system's function only. This study considered GCS ≤ 12 as a severe poisoning group and GCS >12 as a non-severe poisoning group. This cutoff point of GCS was set based on the PSS corresponding to transmission from mild severity to moderate or severe severity.[6]

Statistical analysis

In this study, data with mean (±SD) were presented for quantitative variables or number (percent) for qualitative data. All comparisons were performed using a χ^2 test and a Mann–Whitney test for categorical and continuous data. Missing data were excluded from our analysis. Besides, the statistically significant level was considered less than 0.05. The SPSS software version 18 was used for data analysis.

Results

In the data analysis (n = 135), the patients' mean age was 26.37±18.73 years (minimum age: 1 year, maximum age: 90 years). The demographic and clinical characteristics of these patients are given in Table 2. No chronic diseases such as diabetes mellitus and cardiovascular diseases were recorded in the patients' medical history. The vital signs of patients included mean of heart rate 82.50±15.76 (ranged: 30–140 beats/min), respiratory rate 16.95±4.61 (ranged: 10–41 breaths/min), systolic blood pressure 112.39±17.59 (ranged: 70–180 mmHg), diastolic blood pressure 72.63±11.31 (ranged: 60–120 mmHg), and temperature 36.87±0.42 (ranged: 36–39°C). The mean dose of baclofen ingestion was 215.47 ± 186.06 mg (ranged: 20–1000 mg).

One hundred and seventeen patients (86.7%) had CNS involvement symptoms, and the most common finding was drowsiness (n = 53, 45.3%). There was no patient with a seizure. Nine of the 135 patients (6.6%) had cardiovascular symptoms. All patients had normal kidney function. Four patients had alcohol consumption with baclofen ingestion. Thirty-five (25.9%) and 12 (8.9%) patients were classified as PSS 3 and PSS 2, respectively. Acute respiratory failure was observed in 36 patients (26.7%) who were admitted to intensive care unit (ICU) and had mechanical ventilation. Case fatality rate of baclofen poisoning was 2.96% (four patients died). Three of them were females aged 8, 12, and 17 years, and one case was a man 36 aged years with opioid addiction.

Among the 135 patients, 47 patients (34.8%) had GCS ≤ 12 and 88 patients (65.2%) had GCS>12. Demographic characteristics and clinical findings of the severe and non-severe groups are presented in Table 3. There was a significant difference in baclofen dose between the patients with GCS ≤12 and patients with GCS >12 (302.61 ± 236.40 vs. 162.21 ± 121.02 mg, $P < 0.001$). The time between drug ingestion and admission to the hospital emergency department was in the range of 1–28 h. Four deaths (2.9%) were observed at the hospital on the day after admission. The patients in the severe poisoning group were ventilated ($P < 0.001$). There is no significant difference regarding age, sex, and reason for consumption [Table 3]. No hepatic side effects related to baclofen have been reported.

Discussion

The majority of the studied patients were young and female. The intentional ingestion of baclofen was more common than accidental use. The most common CNS findings were drowsiness, and only a low percentage of the patients had cardiovascular involvement. The majority of these patients had PSS 1 and high GCS (more than 12). A low percentage of them had respiratory failure and received mechanical ventilation. We found four dead cases on the first day of admission that was due to cardiac arrest.

Some studies on the severity of baclofen poisoning led to respiratory failure, but no death was reported,[13-15] so that the proportion of mechanical ventilation was less in this study than in the previous studies. This drug can decrease the seizure threshold, especially in patients with a dependency on alcohol.[6,16] The minimal toxic dose of baclofen is usually more than 200 mg.[7] Some studies reported 300 mg or more in alcohol use disorder,[13,17-19] while the researchers had observed fewer doses than them.

The obtained findings are similar to those previously published, of which intentional attempts are more common in the baclofen overdose, with a difference that the majority of these patients were females but in other studies majority were males due to alcohol use disorders.[1,19,20] The most common clinical findings are drowsiness and depression of GCS in line with other studies.[2,21] The patients are successfully treated with supportive care such as gastric lavage and charcoal. Sometimes they should be managed in intensive supportive care and mechanical ventilation. There is no specific antidote for baclofen.[7] Some physicians give flumazenil and/or physostigmine, but they have no reliable baclofen poisoning effectiveness.[22] The use of hemodialysis is suggested as an appropriate treatment in baclofen poisoning patients with or without renal failure.[23,24]

Table 1: Classification of poison severity score based on symptoms and signs of various organs

Organ	None 0	Mild 1	Moderate 2	Sever 3	Fatal 4
	No symptoms or signs	Mild transient and spontaneously resolving symptoms	Pronounced or prolonged signs or symptoms	Severe or life-threatening	Death
Nervous system		Vertigo, tinnitus, ataxia Mild extrapyramidal symptoms Paresthesia	Unconsciousness with appropriate response to pain Confusion, agitation, hallucinations, delirium Infrequent, generalized, or local seizures	Deep coma unresponsive to pain Extreme agitation Generalized seizures, status epilepticus	
Respiratory system		Irritation, coughing, breathlessness, mild dyspnea, mild bronchospasm Chest X-ray: abnormal with minor or no symptoms	Prolonged coughing, bronchospasm, dyspnea, stridor, hypoxemia requiring extra oxygen Chest X-ray: abnormal with moderate symptoms	Manifest respiratory insufficiency airway obstruction, pulmonary edema, ARDS, pneumonitis Chest X-ray: abnormal with severe symptoms	
Cardiovascular system		Isolated extrasystoles Mild and transient hypo/hypertension	Bradycardia (HR 40–50 in adults) Tachycardia (HR 140–180 in adults) Chest pain Conductance, disturbance Hypertension Hypotension	Bradycardia (HR < 40 for adults) Tachycardia (HR > 180 for adults) Cardiac arrest	
Gastrointestinal tract		Vomiting, diarrhea, pain	Pronounced or prolonged vomiting, diarrhea, pain ileus, dysphagia	Massive hemorrhage, perforation severe dysphagia	
Metabolic imbalance		Mild acid–base disturbances Mild electrolyte and fluid disturbances Mild hypoglycemia Hyperthermia of short duration	More pronounced acid–base disturbances More pronounced electrolyte and fluid disturbances More pronounced hypoglycemia Hyperthermia of longer duration	Severe acid–base disturbances Severe electrolyte and fluid disturbances Severe hypoglycemia	
Renal		Minimal proteinuria/hematuria	Massive proteinuria/hematuria renal dysfunction	Renal failure	
Muscular system		Mild pain, tenderness	Pain, rigidity, cramping, fasciculations Rhabdomyolysis	Intense pain, extreme rigidity, extensive cramping, fasciculations Rhabdomyolysis with complications	
Blood		Mild hemolysis Mild methemoglobinemia	Hemolysis More pronounced methemoglobinemia Coagulation disturbances without bleeding Anemia, leukopenia, thrombocytopenia	Massive hemolysis Severe methemoglobinemia Coagulation disturbances with bleeding Severe anemia, leukopenia, thrombocytopenia	
Liver		Minimal rise in serum enzymes	Rise in serum enzymes, no diagnostic, biochemical, or clinical evidence of liver dysfunction	Rise in serum enzymes, biochemical or clinical evidence of liver dysfunction	
Local effects on skin		Irritation, first-degree burns	Second-degree burns in 10–50% of body surface or third-degree burns	Second-degree burns in >50% of body surface or third-degree burns	
Local effects on eye		Irritation, redness, lacrimation, mild palpebral edema	Intense irritation, corneal abrasion Minor (punctate) corneal ulcers	Corneal ulcers (other than punctate), perforation	

The withdrawal complication of baclofen is found in chronic use that does not depend on its dose and may occur with various signs such as acute psychosis, spasticity, status epilepticus, pruritus, hyperthermia, rhabdomyolysis, and even death.[18,25] The current study did not find withdrawal signs except for one patient.

Table 2: Demographic data and clinical characteristics of the patients with baclofen poisoning

Variables	Number (%)
Gender	
Female	92 (68.1)
Male	43 (31.9)
Cause of poisoning	
Accidental	45 (33.3)
Intentional	90 (66.7)
Marital status	
Unmarried	99 (73.3)
Married	36 (26.7)
Glasgow coma score (GCS)	
GCS≤12	43 (32.8)
GCS>12	88 (67.2)
CNS symptom	
Drowsiness	53 (45.3)
Deep coma	35 (29.9)
Lethargy/fatigue	29 (24.8)
Cardiovascular symptom	
Bradycardia (<60 beats/min)	7 (5.2)
Tachycardia (>100 beats/min)	11 (8.1)
Hypotension (<90/60 mmHg)	4 (2.9)
Hypertension (>140/90 mmHg)	8 (5.9)
Missing data	4 (2.9)
Poison severity score (PSS)	
PSS 0	33 (24.4)
PSS 1	51 (37.8)
PSS 2	12 (8.9)
PSS 3	35 (25.9)
PSS 4	4 (3.0)
Mechanical ventilation*	36 (26.7)

*Acute respiratory failure was considered as need of intubation/ventilation, with respiratory rate <10 breaths/min, PaO_2<60 mmHg (with oxygen supply), $PaCO_2$>50 mmHg

One of the effects suggested by baclofen poisoning is to alter glucose homeostasis. Some studies described that GABA agonists such as baclofen act on pancreas function *in vivo* and reduce blood glucose level in diabetic rats.[26,27] One study showed increased blood glucose levels on day 1 and reduced glucose levels on days later.[28] The biochemical analysis shows an almost significant association with the severity of baclofen poisoning and blood glucose level. It is proposed that baclofen has a possible effect on glucose levels, but its mechanism is still unknown. Further studies require explaining this subject.

As baclofen poisoning has no specific symptoms, its diagnosis is usually based on patients' history and clinical findings. Therefore, physicians must mind to baclofen prescription and reduce high dose/daily in alcohol-dependent patients and patients with neurological indications with a mental illness history.

Limitations

Some limitations of this study were due to retrospective cross-sectional study. This research depends on chart review that was originally not designed to collect data for it and lacked some information such as psychosocial status, follow-up of the patients after recovery, and signs of withdrawal. Data of study were analyzed using a total sample size without excluding four patients who had consumed alcohol due to a small number that was statistically not significant. However, this study can be noticeable and essential due to patients' size with an overdose of baclofen alone in a poisoning center in Tehran.

Conclusion

Baclofen overdose is relatively rare, and diagnosis is based on clinical evidence. The poisoning outcome is related to the

Table 3: Comparison of some variables between patients with severe poisoning and non-severe poisoning

Variable	GCS≤12 (severe group) *n*=47	GCS>12 (non-severe group) *n*=88	*P*-value*
Age (years±sd)	24.66 ± 14.72	27.33 ± 20.83	0.910
Female (*n*, %)	35 (74.5)	57 (64.8)	0.332
Male (*n*, %)	12 (25.5)	31 (5.2)	
Accidental ingestion (*n*, %)	14 (29.8)	31 (35.2)	0.702
Intentional ingestion (*n*, %)	33 (70.2)	57 (64.8)	
Death (*n*, %)	4 (100.0%)	0 (0.0%)	0.015
Heart rate (beats/min)	80.22±17.31	83.45±14.90	0.350
Respiratory rate (breaths/min)	16.91±5.82	16.94±3.89	0.258
Dose of baclofen	302.61 ± 236.40	162.21 ± 121.02	<0.001
Blood glucose (mg/dL)**	135.16 ± 56.20	113.72 ± 30.88	0.050
Aspartate aminotransferase (AST)**	20.73±13.90	22.16±18.31	0.929
Alanine aminotransferase (ALT)**	21.76±8.08	25.43±14.22	0.290
Mechanical ventilation (*n*, %)	34 (72.3)	2 (2.4)	<0.001
Interval ingestion-admission (h)	6.16±3.79	6.92±5.83	0.947

*The significant level was considered less than 0.05

**The reference range of blood glucose <140 mg/dL, AST≤40 U/L, ALT≤ 35 U/L

Quantitative data were analyzed with the Mann–Whitney test, and qualitative data were tested with a χ^2 test

supposed ingested dose and the severity of clinical findings and consciousness level.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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