ORİJİNAL ARAŞTIRMA ORIGINAL RESEARCH

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Overview of Our Cases with Acute Methanol Intoxication: Descriptive Research

Akut Metanol Zehirlenmesi Olgularımıza Genel Bakış: Tanımlayıcı Araştırma

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ABSTRACT Objective: Methanol intoxication is common, especially in fake alcohol production. Its metabolic products can cause acidosis, blindness, and death. In our retrospective study, we aimed to share our experiences in managing 60 patients intoxicated with methyl alcohol. **Material and Methods:** Sixty cases of methanol intoxication, whose records were accessible at Mersin University Faculty of Medicine, Mersin City Training and Research and Toros State Hospitals hospital between 01.01.2017 and 31.12.2019, meeting our criteria, were included in our study. Patients whose data could not be reached and patients with cancer, trauma, hematological disease, acute infection, and immunosuppressive drug use were excluded. **Results:** The mean age of our patients was 51.66±12.09 years, and 88.3% of them were male. While 3.3% of the cases used it for suicide, 96.7% were accidentally intoxicated. The most common complaints on admission were visual impairment in 70% (42), changes in consciousness in 13.3% (8), nausea and vomiting in 10% (6), and seizures in 6.7% (4). In addition to general treatment principles and ethyl alcohol treatment administered to the patients, intermittent hemodialysis (IHD) was applied to 44 patients, while continuous renal replacement therapy (CRRT) to 6 patients. The rate of patients followed up with a mechanical ventilator was 43.3% (34), the mean length of stay in the intensive care unit was 15.11±33.67 days (1-187), and the mortality rate was 35% (21). In terms of morbidity, cognitive dysfunction (e.g., tremor, balance disorder, withdrawal syndrome) was detected in 4 patients, and vision loss developed in 17 of 41 patients with visual impairment. **Conclusion:** Ethyl alcohol administration, IHD and CRRT are specified as emergency approaches in methanol intoxication to correct metabolic acidosis. We think that emergency treatment administration in methanol intoxication is effective on patient outcomes, but the amount of methyl alcohol taken and the duration of admission to the hospital also affect morbidity and mortality rates.

Keywords: Critical care; methanol; alcoholic intoxication; dialysis

ÖZET Amaç: Metanol zehirlenmesi, özellikle sahte içki yapımında sıkça görülmektedir. Metabolik ürünleri asidoza, körlüğe ve ölüme neden olabilmektedir. Retrospektif olarak gerçekleştirdiğimiz çalışmamızda, metil alkol zehirlenmesi olan 60 hastanın yönetimi konusundaki deneyimlerimizi paylaşmayı amaçladık. **Gereç ve Yöntemler:** Çalışmamıza 01.01.2017-31.12.2019 tarihleri arasında Mersin Üniversitesi Tıp Fakültesi, Mersin Şehir Eğitim ve Araştırma Hastanesi ve Toros Devlet Hastanesinden kayıtlarına ulaşılabilen, kriterlerimize uyan 60 metanol zehirlenmesi olguları dâhil edildi. Kayıtlarına ulaşılamayan hastalar, kanser, travma, hematolojik hastalık, akut enfeksiyon ve immünsupresif ilaç kullanımı olanlar hariç tutuldu. **Bulgular:** Hastalarımızın yaş ortalaması 51,66±12,09 yıl olup, %88,3'ü erkek idi. Olguların %3,3'ü intihar amacıyla kullanmışken, %96,7'si kazara zehirlenmiştir. Geliş şikâyetleri en sık görme bozukluğu %70 (42), bilinç değişikliği %13,3 (8), bulantı ve kusma %10 (6) ve nöbet geçirme %6,7 (4) olarak tespit edilmiştir. Tüm hastalara genel tedavi prensipleri ve etil alkol tedavisi uygulanmış; 44 hastaya aralıklı hemodiyaliz [intermittent hemodialysis (IHD)] uygulanırken, 6 hastaya sürekli renal replasman tedavisi (SRRT) uygulanmıştır. Mekanik ventilatör ile takip edilen hasta oranı %43,3 (34), ortalama yoğun bakım yatış süresi 15,11±33,67 gün (1-187) olup, mortalite oranı ise %35 (21) olarak bulunmuştur. Morbidite açısından 4 hastada kognitif fonksiyon bozukluğu (tremor, denge bozukluğu, yoksunluk sendromu vb.) saptanmış, görme bozukluğu şikâyeti ile gelen 41 hastanın 17'sinde ise görme kaybı gelişmiştir. **Sonuç:** Metanol intoksikasyonunda, metabolik asidozun düzeltilmesi için etil alkol uygulanması, IHD ve SRRT uygulaması acil yaklaşımlar olarak belirtilmektedir. Metanol intoksikasyonunda acil tedavi uygulanmasının, hasta sonuçları üzerine etkili olduğunu ancak alınan metil alkol miktarının ve hastaneye geliş süresinin de morbidite ve mortalite oranları üzerinde etkili olduğunu düşünmekteyiz.

Anahtar Kelimeler: Yoğun bakım; metanol; alkol zehirlenmesi; diyaliz

Methanol is an alcohol used in industry and is known as wood spirit. Methanol causes suicidal or accidental intoxication due to the consumption of fake alcohol. It is vital to identify as it can have toxic effects even when taken in small quantities. While methanol itself causes initial symptoms, methanol metabolites, mostly formic acid, cause persistent neurological sequelae.[1]

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In cases with a history of fake alcohol consumption, the toxic blood methanol level (>20 mg/dL) is diagnosed according to the gas chromatography method. Severe metabolic acidosis accompanied by increased anion gap and osmolar gap supports the diagnosis.[2] However, both the non-specific clinical characteristics and the emergence of the findings after the latent period cause a delay in diagnosis. Also, another reason for the delay in diagnosis is the lack of methanol level analysis facilities in many hospitals in the country.[3]

In this study, we aimed to share our experiences of patients hospitalized in tertiary anesthesia intensive care unit (ICU) due to methyl alcohol intoxication according to their treatments and mortality.

MATERIAL AND METHODS

The study included 60 patients who were followed up with the diagnosis of acute methanol intoxication in the ICU at Mersin University Faculty of Medicine, Mersin City, and Toros State Hospitals. The research was conducted in accordance with the Helsinki Declaration principles. Approval numbered 2020/173 was obtained from Mersin University Faculty of Medicine Ethics Committee on 19/02/2020. The medical records, laboratory and radiological findings and application complaints of the patients were evaluated retrospectively between 01.01.2017 and 31.12.2019. When the hospitalization time of our patients was examined, it was determined that they were admitted to the emergency room within 24-48 hours after alcohol consumption. Patients' demographic data (age, gender), Glasgow Coma Scale (GCS), Acute Physiology and Chronic Health Evaluation (APACHE II), blood gas values, mechanical ventilation requirement, and length of stay in (ICU), medical and adjunctive therapies intermittent hemodialysis (IHD), and continuous renal replacement therapy (CRRT) were examined. Patients with cancer, trauma, hematological disease, acute infection, and immunosuppressive drug use, and patients whose data could not be reached were excluded.

Mann-Whitney U and Student t-tests were used to compare data in statistical analysis. Chi-square test was used to compare categorical variables.

RESULTS

Of the 72 patients followed up with methanol intoxication during the 2-year period, 60 were included in the study (2 patients were excluded due to hematological diseases, and 10 patients as their records could not be reached). Of the 60 patients included in the study, 88.3% were male, 11.7% were female, and the mean age of all patients was 51.66±12.09 years. All intoxications were due to oral intake. While 3.3% of our patients (2 patients) took methanol for suicide, the remaining 96.7% (58 patients) were accidentally intoxicated (Table 1).

The mortality rate of our patients was 35% (21 patients). The rate of patients followed up with a mechanical ventilator was found as 43.3% (26 patients), the length of stay in the ICU was 15.11±33.67 (Table 1).

When the presenting complaints were evaluated, the most common complaints were visual impairment in 70%, changes in consciousness in 13.3%, nausea and vomiting in 10% and seizures in 6.7% (Table 2). Supportive treatment (e.g., bicarbonate and liquid)

TABLE 1: Patient characteristics.

Gender, female/male, n (%)	7 (11.7)/53 (88.3)
Age, year, mean±SD	51.66±12.09
Intoxication reason, accidental/suicide, n (%)	58 (96.7)/2 (3.3)
Mortality, alive/exitus, n (%)	39 (65)/21 (35)
ICU stay, day, mean±SD	15.11±33.67
MV requirement, yes/no, n (%)	26 (43.3)/34 (56.7)

SD: Standard deviation; ICU: Intensive care unit; MV: Mechanical ventilation.

TABLE 2: Complaints of patients and given treatments.

	Patients (n=60)
Complaints	
Nausea and vomiting, n (%)	6 (10)
Visual loss, n (%)	42 (70)
Cognitive dysfunction, n (%)	8 (13.3)
Seizure, n (%)	4 (6.7)
Treatments	
Ethyl alcohol, given/not given, n (%)	55 (91.7)/5 (8.3)
Folat, given/not given, n (%)	5 (8.3)/55 (91.7)
Renal replacement therapy, done/not done, n (%)	50 (83.3)/10 (16.7)

was administered to all patients. As an antidote, 55 (91.7%) patients were given 10 mL/kg 30 minimum. loading, 1 mL/kg/hour maintenance dose of 10% intravenous ethyl alcohol, and 55 (91.7%) patients were given folate (Table 2).

Since the methanol level cannot be measured, IHD is initiated in all patients with resistant acidosis in blood gas, visual impairment, electrolyte disorders or acute kidney injury, and deteriorated general condition. We also administered renal replacement therapy to 80% of our patients (Table 2). While IHD was performed on most of our patients (44), CRRT was initiated on 6 patients who could not undergo IHD due to poor general condition and hypotension.

APACHE II scores were significantly higher in intubated patients and dying patients (p<0.001, p=0.002) (Table 2). Besides, patients with an APACHE II score of <20 were found to have shorter ICU stays (p=0.040) (Table 3).

Blood gas levels and GCS scores were evaluated in Table 4. pH and HCO_3 levels were statistically lower in mortal patients (p=0.000) (Table 4). When the relationship between the GCS levels with mortality was examined, it was observed that mortality was 80% in those with GCS 3-8, 57.1% in those with GCS 9-12, and 3% in those with GCS 13-15 (p=0.001) (Table 4). When we made a posthoc analysis of GCS to understand which group the difference originated from, a significant difference was found between Group 1-3 (p=0.000) and Group 2-3 (p=0.000), and when we made a comparison between Group 1-2 (p=0.235), it was observed that there was no significant difference.

DISCUSSION

The use of alcoholic beverages with methanol has caused acute intoxication outbreaks in many countries.[4,5] In our country, laws and regulations prohibit the use of methyl alcohol in alcoholic beverages and colognes and require the use of ethyl alcohol. Illegal alcoholic beverage production and consumption are of great importance in Turkey and the world. According to the 2010 report of the World Health Organization Global Alcohol and Health Information System, 30% of the alcohol consumption in Turkey cannot be recorded.[6]

TABLE 3: Evaluation of APACHE II scores.

	Alive (n=39)	Exitus (n=21)	p value
APACHE II scores, median (minimum-maximum)	15 (20-26)	20 (12-29)	0.002*
	With MV (n=26)	Without MV (n=34)	
	20 (12-29)	15 (10-26)	0.000*
	APACHE<20 (n=41)	APACHE≥20	
ICU stay, day, median (minimum-maximum)	4 (1-187)	5 (1-131)	0.040*

*Mann-Whitney U; APACHE II: Acute Physiology and Chronic Health Evaluation; MV: Mechanic ventilation; ICU: Intensive care unit.

TABLE 4: Relationship of pH, PaO_2, HCO_3 levels and GCS scores with mortality.

	Alive (n=39)	Exitus (n=21)	p value
pH	7.2 (6.79-7.40)	6.9 (6.5-7.3)	0.000*
PaO_2	72 (65-90)	69 (45-86)	0.083*
HCO_3	15 (2.6-35)	6.9 (2.20-21.70)	0.000*
GCS			
GCS 3-8	4	16	0.001#
GCS 9-12	3	4	
GCS 13-15	32	1	

*Mann-Whitney U; #Chi-square; Datas were given as median (minimum-maximum) and mean.
PaO_2: Partial arterial oxygen pressure; HCO_3: Bicarbonate; APACHE II: Acute Physiology and Chronic Health Evaluation; GCS: Glasgow Coma Scale.

Accidental ingestion is often due to the cheaper methanol used in alcohol production. Most of the intoxication is caused by illegal producers offering products containing methanol or by accidentally using methanol by groups that produce handmade alcohol at home.[7] In our study, 3.3% of patients took methanol for suicide whereas 96.7% of them were accidentally intoxicated and mortality rate was 35% unfortunately.

Depending on its intake with ethanol, the onset of symptoms ranges from 40 minutes to 72 hours, with an average of 24 hours.[8] The toxic metabolite formic acid is responsible for retinal and optic nerve damage.[9] This damage causes reversible visual disturbances in most patients. Also, permanent visual sequelae have been described following severe intoxication.[10] Central nervous system symptoms are headache, lethargy, confusion, and Parkinson-like extrapyramidal symptoms. The prognosis of the disease is related to the amount of methanol consumed, the degree of metabolic acidosis, the amount of formic acid accumulated in the blood, and the presence of coma or seizure at presentation.[11]

Our study determined that most of the discharged patients referred to the hospital with complaints of nausea/vomiting and visual impairment, while the patients who died were mostly those admitted with unconsciousness and seizures. Nausea/vomiting and visual impairment are symptoms disturbing the patients and suggest that they cause early admission and hospitalization.[12]

In treating acute methanol intoxication, fomepizole and ethanol, which have a higher affinity for alcohol dehydrogenase enzyme than methanol, can be used. Thus, the conversion of methanol into toxic metabolites can be prevented.[8] Other treatments include gastric lavage, sodium bicarbonate, folic acid, and hemodialysis. In methanol intoxication, if treatment is started immediately with early diagnosis, mortality can be reduced. However, neurological sequelae may remain in patients despite appropriate treatment.[13]

Because of the high cost, limited availability, and short shelf life of fomepizole, ethanol is often used. Although ethanol is more accessible and cheaper, it has several potential side effects such as sedation and respiratory depression.[14]

Hemodialysis is an essential part of treatment because of its ability to remove methanol and toxic metabolites from the body.[8] It corrects metabolic acidosis and electrolyte disturbances, thus reducing stay in hospital.

In many studies, IHD is the first emergency treatment approach applied to patients. In the study conducted by Zakharov et al., it was stated that IHD is superior to CRRT for faster methanol and formic acid elimination, and if CRRT is the only treatment available, elimination is higher with higher blood and dialysate flow rates.[15] According to Peces et al., initiation of preemptive IHD as soon as possible in alcohol intoxication is correlated with a decrease in mortality rates.[16] In our study, metabolic acidosis (low pH), low HCO_3, low GCS (GCS≤8), and increased APACHE II scores were found to be associated with poor outcomes in methanol intoxication. When the relationship between the GCS levels with mortality was examined, it was observed that mortality was 80% in those with GCS 3-8, 57.1% in those with GCS 9-12, and 3% in those with GCS 13-15 (p=0.001). It was determined that as the GCS increased, mortality decreased significantly. Imaging with computed tomography and magnetic resonance imaging (MRI) are among the diagnostic tests. In the study conducted by Jain et al., the most critical finding in MRI in methanol intoxication was hemorrhagic putaminal necrosis.[13] Radiological imaging was performed in 29 patients with GCS below 15, hypoxemic encephalopathy was found in 5 of our patients, intracerebral hemorrhage in 2, and subarachnoid hemorrhage in 1st brain death developed in 2 patients with intracerebral hemorrhage. No pathology was determined in 21 patients who underwent imaging. Imaging examination was requested from our patients who had visual impairment and impaired neurological examination. Although neuroimaging does not affect the treatment much, it may be useful in predicting the patient's prognosis.[3] Considering the follow-up of our patients after intensive care, it was determined that 17 of 41 patients who came with the complaint of

visual impairment developed vision loss, and 4 patients had cognitive dysfunction (e.g., tremor, balance disorder, withdrawal syndrome).

When we evaluated the morbidity rates, it was determined that 39 (65%) patients were discharged. Fourteen of the discharged patients had no sequelae, 17 patients were discharged with vision loss, three patients were sent home as care patients, and 1 patient was discharged to a nursing home.

CONCLUSION

Patients with a clinical history of alcohol intake and deep metabolic acidosis in blood gas should make us think about methyl alcohol intoxication. In unconscious patients with an unknown history, diagnosis becomes difficult when the initial complaints are similar to other similar clinical conditions and when laboratory tests used in diagnosis are not available.[14] Despite advances in treatment, methanol intoxication is one of the most important causes of intoxication-related deaths due to difficulties in diagnosis and late admission to the hospital.[17]

In conclusion, we think that early initiation of antidote and elimination treatment approaches in methyl alcohol intoxication can result in more effective results and decrease morbidity and mortality.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Bilge Banu Taşdemir Mecit;* ***Design:*** *Ali Altunkan;* ***Control/Supervision:*** *Ali Altunkan;* ***Data Collection and/or Processing:*** *Ezgi Ata, Bahar Aydınlı, Harun Özmen;* ***Analysis and/or Interpretation:*** *Ali Altunkan, Bilge Benu Taşdemir Mecit;* ***Literature Review:*** *Bilge Banu Taşdemir Mecit, Hanife Kara;* ***Writing the Article:*** *Bilge Banu Taşdemir Mecit;* ***Critical Review:*** *Ali Altunkan.*

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