



Accidental Methanol Poisoning At A Tertiary Care Centre Of North India: A Retrospective Observational Study

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Abstract

Background: Methyl alcohol poisoning most commonly occurs via oral ingestion of illicit or adulterated liquors or as ethanol substitution, also absorbed transdermally or by inhalation An unfortunate "Hooch" tragedy occurred in and around different localities of Aligarh District in the months of May-June 2021, where in several people consumed illicit liquor which was dumped by an unknown truck.

Objective: The purpose of this study was to assess the clinical parameters and effect of early intensive management including Hemodialysis on the patient outcome parameters.

Methods: A total of 42 patients presented to the Emergency department of our hospital via referral, of which 2 died during the primary management itself. The rest of the 40 patients were given 3 sessions of Dialysis for 3 days consecutively.

Results: At presentation, majority of the patients reported Gastrointestinal symptoms like Nausea and Vomiting, while Abdominal Pain was reported by 61.9%. Visual symptoms like Blurred Vision was complained by 66.7%, however, Blindness was present in only 14.3% (n=6). There was a significant improvement in pH from admission to discharge [Median 7.19 (IQR 7.10-7.27)] which was significant on Wilcoxon signed rank sum test (W=-3.65, P0.001). The most dramatic effects on the Bicarbonate levels were HCO₃ on admission was 9.60 (5.23-17.48) while on discharge it was 26.70 (24.55-29.20) (W = -5.51, P0.0001). The most significant effect was on the pH (P0.001), HCO₃, HCO₄, and Bicarbonates (P=0.001).

Conclusion: Timely Dialysis is very effective in preventing mortality from acute methanol poisoning as well as it significantly improves morbidity.

Keywords: Methanol, Alcohol Dehydrogenase, Formaldehyde, Formic Acid, High Anion gap Metabolic Acidosis

Introduction

Methyl alcohol or methanol or wood alcohol, is a toxic chemical, colorless and volatile having specific gravity of 0.81, boiling point of 650 C and molecular weight of 32.04 g/mole. It is often found in significant concentration in automobile antifreeze,

de-icing solutions, windshield wiper fluid, varnishes, paint thinner and many other industrial products. Methyl alcohol poisoning most commonly occurs via oral ingestion of illicit or adulterated liquors or as ethanol substitution, also absorbed transdermally or

by inhalation. Methyl alcohol has a narcotic effect on central nervous system; however it is a substance of low toxicity by itself. After an oral ingestion it is readily absorbed by gastrointestinal tract. Up to 90-95% of ingested methanol is metabolized in the liver via alcohol dehydrogenase (ADH) aldehyde dehydrogenase (ALDH) systems in the process known as “lethal synthesis”. Products of this metabolism pathway – formaldehyde and formic acid are responsible for the acute toxicity, as they cause severe metabolic acidosis, lead to eye and Central nervous system damage and are responsible for the death of poisoned persons. Patients may take a few hours to 2 days after ingestion to become symptomatic. It had been estimated that a dose of 1.2mL/kg is lethal for humans. Mortality in methanol Poisoning ranges from 18-44%. The survivors may recover completely but many often suffer from permanent visual and neurological sequelae. Reports of outbreak of methyl alcohol poisoning from different parts of India revealed that the victims are poor people in rural areas with lack of infrastructures and tertiary care facilities resulting in high mortality.[1-6].

An unfortunate “Hooch” tragedy occurred in and around different localities of Aligarh District in the months of May-June 2021, wherein several people consumed illicit liquor which was dumped by an unknown truck. Consequently, forty two patients presented to the Emergency department of our hospital via referral. This study was done to assess the clinical parameters and effect of early intensive management including Hemodialysis on the patient outcome parameters.

Material And Methods

It is a Single-Center, Retrospective, Observational, Case-series study.

Ethical approval was taken from Institutional Ethics Committee before commencing the study. All of the relevant case sheets were recalled from the Hospital Records and patient details regarding presenting symptoms, duration of intoxication, physical examination findings, Arterial blood gas, Serum Electrolytes, Complete Blood Count, Renal Function tests and Liver Function tests were studied along with the mode of therapy instituted including Hemodialysis. Morbidity and Mortality were studied

in terms of improvement or deterioration of patients clinical and/or laboratory parameters.

Patients with history of Methanol Poisoning along with visual symptoms or altered mental status or gastro-intestinal symptoms or respiratory distress or oligo-anuria were included. Exclusion criteria consisted of patients with unconvincing history of Methanol ingestion or known case of Diabetes Mellitus, CKD, COPD or Stroke.

Serum methanol levels could not be done. Anion gap could not be calculated as well, since chloride estimation was not available in emergency department.

As soon as the information of mass poisoning was received, the emergency physicians were alerted, the critical care and nephrology teams were also actively involved. Upon arrival, above mentioned blood work up was sent, and active resuscitation and management was instituted. None of the patients needed intubation. Irrespective of the severity of metabolic acidosis, upon the recommendation of the nephrologist, all patients were given Hemodialysis therapy. Interim management was done with intravenous fluids, iv thiamine 300mg, iv folinic acid 50mg and iv calcium gluconate (10%) 10mL over 10 minutes. Intravenous sodium bicarbonate (8.4%) 100mL was given to all patients to buffer the metabolic acidemia.

Oral or Intravenous Ethanol and Fomepizole therapy were not given because of unavailability and lack of previous experience.

The standard indications of Hemodialysis in Methanol Poisoning include ingested amount more than 30mL, or a Serum methanol concentration of >20mg/dL, or persistent metabolic acidosis (pH <7.30, HCO₃<15), or presence of ophthalmological symptoms/signs. However, in our case, we instituted Hemodialysis to all patients for two and a half hours for three consecutive days using a high flux F60/F80 dialyzer with blood flow at 200 mL/min and dialysate flow at 450 mL/min.

Statistical analysis was done using SPSS. The continuous variables are presented in the form of Mean and Standard Deviation or Median (IQR), as applicable. The categorical variables are presented as

proportions or percentages. Wilcoxon signed rank sum test has been applied to test statistical significance of pre-post continuous variables. To compare categorical pre-post values, McNemar's Chi square test has been applied.

Result

A total of 42 patients were included in the study, of which 2 died during the primary management itself. Both patients who died had presented with severe metabolic acidosis with a pH of 6.83 and 6.99. While one could not be started on dialysis, the other expired during dialysis. The rest of the 40 patients were given 3 sessions of Hemodialysis for 3 days consecutively. At presentation, majority of the patients reported Gastrointestinal symptoms like Nausea and Vomiting (71.4%, n=30), while Abdominal Pain was reported by 61.9% (n=26). Visual symptoms like Blurred Vision was complained by 66.7% (n=28), however, Blindness was present in only 14.3% (n=6). Neurological Symptoms like Drowsiness was observed in 52.4% patients (n=22), whereas Altered Sensorium was seen in 40.5% (n=17). (Table 1a).

On examination, the mean Pulse rate was 91.12 ± 14.16 (Median 90), Respiratory Rate was 21.21 ± 2.81 (Median 20), Oxygen Saturation was 96.14 ± 1.97 (Median 96), and Temperature was 98.18 ± 1.04 (Median 98.6), all suggestive of the fact that vital parameters were largely within normal limits at presentation. The average GCS of the patients was 13.62 ± 1.61 (Median 15). Pupils were Fixed and Dilated in 16.7% (n=7) patients, sluggishly reacting in 47.6% (n=20), however, they were normal sized and normally reacting in 35.7% (n=15). Funduscopic examination was suggestive of abnormal findings like Disc Hyperemia, Disc pallor, RNFL edema, Arteriolar attenuation in 31% patients (n=13). (Table 1a and Table 1b).

All patients were rapidly investigated for Blood Gas Analysis, Complete Blood Count, Renal Function & Liver Function. The mean pH at presentation was 7.16 ± 0.14 , whereas Bicarbonate (HCO_3) was 10.69 ± 6.54 (Median 8.95). Sodium and Potassium were mostly within normal range (IQR 136.75-144 for Na^+ , IQR 3.18-4.53 for K^+). Calcium was 0.83 ± 0.20 (IQR 0.71-0.98). Mean Lactate at presentation was 2.51

± 1.78 . Average Random Blood Glucose was 123.90 ± 69.63 . Median Total Leucocyte Counts were 8600, Serum Creatinine was 0.99 ± 0.39 (Median 0.84), Blood Urea Nitrogen was 15.5 ± 5.86 , Total Bilirubin was 0.90 ± 0.42 , and Aspartate Aminotransferase was 50.02 ± 30.34 , Alanine Aminotransferase was 48.29 ± 33.98 (Table 1).

On an average, the patients received their first Hemodialysis after 28.99 ± 18.79 hours of consumption of the illicit liquor reflecting the duration of intoxication.

Six patients presented with blindness and were treated with 1000 mg intravenous methylprednisolone pulse therapy for three days followed by oral prednisolone 1 mg/kg for 11 days, in addition to Hemodialysis. All six patients showed improvement at one month of follow up. Three of them showed an improvement of at least 2 lines on

Snellen's chart and two patients improved from doubtful light perception to counting fingers at least 2 metres ahead and one patient improving from perception of light to counting fingers at least 2 metres ahead.

Post Hemodialytic changes were evaluated for pH, HCO_3 , BUN and other parameters. There was a significant improvement in pH from admission [Median 7.19 (IQR 7.10-7.27)] to discharge [Median 7.28 (IQR 7.22-7.39)], which was significant on Wilcoxon signed rank sum test ($W = -3.65$, $P < 0.001$). Hemodialysis, perhaps, had the most dramatic effects on the Bicarbonate levels as HCO_3 on admission was 9.60 (5.23-17.48) while on discharge it was 26.70 (24.55-29.20) ($W = -5.51$, $P < 0.001$). Most parameters except K^+ , Lactate and Glucose improved significantly after Dialysis (Table 2).

We also assessed the difference in normalizing values of pH, HCO_3 , & BUN at discharge. HCO_3 was found to be normal in 87.5% (35/40), at discharge as opposed to 5% (2/40) at admission which was significant (McNemar's Chi square test $P < 0.001$). The pH at discharge was found to be normal in 25% (10/40) as opposed to 7.5% (3/40) at admission. Similarly, BUN at discharge was normal in 90% (36/40), as opposed to 80% (32/40) at admission. However, both pH and BUN normalizing values were not statistically significant (McNemar's Chi square test $P = 0.092$ and $P = 0.344$, respectively).

Discussion

Methanol poisoning has a high fatality rate, which has been linked to treatment delays and a dearth of Hemodialysis (HD) treatments, as can be observed in earlier Indian studies. Similar to the experience of Ravichandran et al. [1], who have described 47 patients with methanol poisoning who were treated fairly early and some of them received HD, achieving a low mortality rate in two patients, our patients' mortality rate was low when they received early and timely dialysis treatment. According to Rathi et al. [7], rapid ethanol administration and the implementation of HD led to the total reversal of methanol symptoms. India has been the center of numerous outbreaks of methanol poisoning [1,2,7-10]. According to Bade and Sapre's [8] descriptions of 11 methanol poisoning patients, two of them were brought in already dead, while the others all passed away within three days. Divekar et al. [9] reported seven patients died out of the 45 methanol poisoning patients who were treated with alkali, ethanol, and supportive measures. According to Krishnamurthi et al. [10], 32 patients died of 87 methanol poisoning patients treated with alkali therapy and supportive measures. In a study by Kumar et al. [2] from Chennai, 67 patients were treated with bicarbonate, ethanol, and folic acid in 2001; 21 patients died, mostly as a result of the lack of arterial blood gas analysis and dialysis. Based on the clinical symptoms and the degree of metabolic acidosis prior to HD, all of our patients experienced a significant degree of poisoning. One of the most significant findings of our study was that all symptoms of methanol poisoning were reversed without any long-term effects, and there was a very low mortality from methanol poisoning as a result of prompt HD

and supportive treatment. These results are in contrast to high death rates reported by other studies [2,8-10] and stands in tandem with the results of Kute et al, [11] who has described 91 patients with methanol poisoning and because of timely Hemodialysis, a mortality of only 3 patients was seen.

The most noticeable abnormality we observed in our patients was metabolic acidosis, likely due to accumulation of Formic acid and Lactic acid [12,13]. Due to their low molecular weight, minimal protein binding, and modest distribution volume, all alcohols

can be effectively eliminated by HD [14]. The most effective way to quickly reduce serum levels of harmful alcohols or to remove organic acid anions such formate is intermittent HD [14]. Due to the delayed availability of serum methanol analysis findings, patients were given bicarbonate, ethanol, and HD based on their clinical characteristics and the presence of metabolic acidosis as indicated by blood gas values.

At blood flows of 100–400 mL/min, HD offers a clearance of 200 mL/min for methanol and 223 mL/min for formate. When compared to endogenous elimination, HD dramatically decreased the half-life of formate elimination [15,16]. Peritoneal dialysis and other types of continuous renal replacement therapy are not advised since they are ineffective at removing toxic alcohols and their metabolites [17,18].

Conclusion

Methanol poisoning presents with Gastrointestinal, Visual and Neurological symptoms. The diagnosis may be delayed because of vague complaints initially. Especially in countries like India where illicit liquor is so rampant or in countries with a social taboo or legal restriction on sale of liquor, patients might hesitate to present on time. Although, Serum methanol levels should ideally be obtained, but a high anion gap metabolic acidosis is sufficient enough to proceed with urgent treatment. High dose intravenous methylprednisolone showed improvement in visual outcome of methanol related optic neuropathy. Timely Hemodialysis is very effective in preventing mortality from acute methanol poisoning as well as it significantly improves morbidity. Thus, it should be a recommended therapy in all methanol Poisoning patients.

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