ORIGINAL RESEARCH

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Methanol Poisoning - Outbreak Dynamics and Therapeutic Uncertainties in Rural India

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Abstract

Objective: Methyl alcohol poisoning in India occurs as explosive outbreaks with mortality rates reaching 20%. Rural hospitals are often ill-equipped and lack expertise in handling such crises. The purpose of this work is to emphasize our experience regarding outbreak dynamics, clinical triage, sociocultural influences impacting treatment, and mortality predictors.

Materials and Methods: This was a hospital-based retrospective descriptive study conducted on 58 methanol poisoned adult patients who were admitted between 14th-16th May 2023. All patients had consumed methyl alcohol adulterated liquor on 13th May 2023, and were admitted to the emergency department at varying time periods. The main outcomes studied were death and permanent visual impairment.

Results: Among 58 victims, 49.2±13.1 years was the mean age. Of the patients, 86.20% were admitted within 48 hours of symptoms, with the median time to admission being 12-24 hours from consumption. The most common presenting symptoms were giddiness (32.75%) and abdominal pain (31.03%). Significant clinical parameters associated with mortality were altered consciousness, shock, and severe acidosis. 85.71% of patients with severe acidosis either succumbed or suffered permanent visual damage. The case fatality rate was 15.51%. Death peaked around 24 to 30 hours (55.56%). The median time to death from consumption was 40 hours, and 78% died by 48 hours.

Conclusion: Methanol poisoning in India is commonly due to adulterated liquor consumption. Baseline triage tools include pH, mental status assessment, respiratory distress, and hemodynamic instability. Ethanol treatment is fraught with risks and might not be socially acceptable. Future outbreaks should be anticipated. Every tertiary care hospital should have standard operating procedures in place and maintain an emergency stock of fomepizole.

Keywords: Methanol poisoning, outbreak, mortality predictors, treatment

Introduction

Methyl alcohol overdosage plagues almost every country on the globe [1]. However, the dynamics of poisoning differ significantly between countries. Whereas in developed nations sporadic cases occur infrequently, in India point source outbreaks are a common occurrence [2]. Consumption of adulterated liquor is the root cause. The dynamics of such an outbreak needs special mention. Outbreaks are explosive, flooding the nearest healthcare facility, which is often ill-equipped to handle the load. What is worse is that mortality ensues with frightening rapidity unless the health care team is triage-trained and has adequate infrastructural support.

Crude mortality rates for methanol poisoning hover between 18-44% [3,4]. The lethal dose has been reported as 50-500 mL [5,6]. A common cause of death appears to be severe acidosis and respiratory failure [7]. The only reliable laboratory markers

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of severity are serum methanol or formic acid levels, which are expensive and require infrastructure and expertise [8,9]. Point-of-care tests with both clinical and laboratory applications with early prognostic capacity are essential to triage patients.

We, at a rural tertiary care hospital, experienced one such outbreak in May of 2023, pushing the entire hospital into crisis mode. A retrospective analysis was conducted in its aftermath, which yielded valuable information to manage future eventualities. We aimed to share our experience with the scientific community with special emphasis on clinical presentation, sociocultural influences that impact treatment, and probable predictors of mortality. We also hope to create awareness among primary care physicians about the lethality of methanol poisoning and feasible treatment strategies in a resource-limited facility.

Materials and Methods

Electronic and manual case records of 58 patients admitted between the 14th and 16th of May 2023 for methanol poisoning were scrutinized for clinical and laboratory data. The outbreak dynamics such as mean time delay for hospital presentation, peak admission rates, mortality peak time, and average time to discharge were documented. Clinical features documented include presenting symptoms, consciousness state, vital signs, systemic and visual examination findings, complications, and treatment provided. Lab parameters documented include complete blood count, biochemical profile, including electrolytes, liver function tests, and arterial blood gas (ABG) analysis. Patients with severe acidosis were defined as those with a pH less than 7.2 at initial examination. Patients were triaged and managed using injection thiamine, injection pyridoxine, injection vitamin B12, tablet folic acid, and alkaline diuresis with injection. Sodium bicarbonate and crystalloids as per standard recommendations. Those with severe acidosis and depressed mentation underwent intermittent hemodialysis.

Ethical Consideration

The study was approved by the Government Villupuram Medical College and Hospital Institutional Ethics Committee (approval number: GVMC/IEC/2023(2)/3, date: 12.12.2023).

Statistical Analysis

Statistical analysis consisted of the Student's t-tests for independent variables and odds ratios, wherever appropriate. Univariate analysis determined the correlation between various tested laboratory investigations and the outcome. Values that showed significant association with mortality on univariate analysis were included in the multiple linear logistic regression model with death as the dependent variable and all associated parameters as independent variables. Statistical analysis was performed using SPSS, version 16 (SPSS, Inc). Statistical significance was set at 0.05.

Result

A total of 58 victims were admitted for consumption of methanol-adulterated liquor. 49.2±13.1 years was the mean age of the patients. Thirty-six (62.06%) developed symptoms within 24 hours of consumption. Fifty (86.20%) were admitted within 48 hours of symptoms; the median time to admission was 12 to 24 hours from consumption. The most common presenting symptoms were giddiness [19 (32.75%)] and abdominal pain [18 (31.03%)]. Triage done at baseline identified 14 patients as critically ill, and these patients were relocated to the intensive care unit (ICU). (8/14) 57.14% of ICU patients suffered mortality, whereas (1/44) 2.27% of non-ICU patients succumbed; the comparison was statistically significant ($p<0.01$). Eight (13.79%) patients had late manifestations (>48 hours) after consumption. The case fatality ratio for this outbreak was 15.51% (9/58). Death peaked around 24-30 hours (55.56%). The median time to death from consumption was 40 hours and 78% died by 48 hours. Significant clinical parameters associated with mortality were altered consciousness, shock, and severe acidosis (Table 1). Lab data included pH <7.2 in 12.07%, electrocardiogram abnormalities in 15.51%, and biochemical alterations in 21/58 or 36.21% of patients. Excluding pH, none were statistically significant. (6/7) 85.71% of patients with severe acidosis succumbed to the illness. The only survivor with pH <7.2 suffered severe morbidity [permanent visual damage (light perception or movement perception only)]. The methanol-poisoned patient with a baseline pH of <7.2 had a 96-fold higher chance of dying than his counterpart with pH >7.2.

Discussion

Although methanol itself is not highly toxic, it is metabolized by alcohol dehydrogenase (ALD) to form toxic metabolites formaldehyde and formic acid, which culminate in metabolic acidosis, blindness, cardiovascular instability, and death [10]. Formic acid, which is the major circulating metabolite, appears to be the key factor responsible for toxicity and death [11]. Inhibition of ALD and, in selected patients, hemodialysis are the traditional treatments for methanol poisoning.

Methanol poisoning in India occurs commonly as point source outbreaks [4,12]. The outbreak at Villupuram affected 58 persons, claimed 9 lives, and left 2 permanently blind. From a clinical standpoint, the time lag between consumption and presentation ranged from 6 to 60 hours, with peak admission rates occurring at 12-24 hours (21 patients) (Figure 1). 86.21% of victims presented within 48 hours of consumption. The implication is to activate and pool the best available resources in this time frame, in the event of future outbreaks. Notable clinical manifestations included giddiness (32.75%), abdominal pain (31.03%), and altered mentation (25.86%). However, only depressed mentation [odd ratio (OR): 48], shock (OR: 0.03), and respiratory distress (OR: 0.07) correlated with mortality.

Table 1. Clinical features and laboratory profile of methanol-poisoned inpatients at a tertiary care hospital and their correlation with outcome

Variables		Alive	Dead	OR	Significance
Headache	Yes	7 (77.8%)	2 (22.2%)	0.58	0.61
	No	42 (85.7%)	7 (14.3%)		
Giddiness	Yes	17 (89.4%)	2 (10.6%)	1.86	0.51
	No	32(82.1%)	7 (17.9%)		
GCS <8	Yes	7 (46.7%)	8 (53.3%)	48	<0.001
	No	42 (97.7%)	1 (2.3%)		
Vomiting	Yes	8 (80%)	2 (20%)	0.68	0.646
	No	41(85.4%)	7 (14.6%)		
Abdominal pain	Yes	17 (94.4%)	1 (5.6%)	4.25	0.249
	No	32 (80%)	8 (20%)		
Dyspnoea	Yes	4 (44.4%)	5 (55.6%)	0.07	0.003
	No	45 (91.8%)	4 (8.2%)		
Shock	Yes	3 (33.3%)	6 (66.7%)	0.03	<0.01
	No	46 (93.9%)	3 (6.1%)		
Diarhoea	Yes	1 (33%)	2 (67%)	0.07	0.06
	No	48 (87%)	7 (13%)		
Palpitation	Yes	3 (75%)	1 (25%)	0.52	0.61
	No	46 (85.2%)	8 (14.8%)		
Hemiodialysis	Yes	13 (81.3%)	3 (18.7%)	1.39	0.68
	No	36 (85.7%)	6 (4.8%)		
ECG abnormality	Yes	11 (78.6%)	3 (21.4%)	1.73	0.52
	No	38 (86.4%)	6 (13.6%)		
CBC abnormality	Yes	9 (75%)	3 (25%)	0.62	0.61
	No	40(86.9%)	6 (13%)		
LFT abnormality	Yes	7(63.6%)	4 (36.4%)	0.59	0.68
	No	42 (89.4%)	5 (10.6%)		
ABG, pH <7.2	Yes	1 (14.3%)	6 (85.7%)	96	<0.001
	No	48 (94.1%)	3 (5.9%)		
HCO_3 <10 mEq/L	Yes	5 (38.5%)	8 (61.5%)	70.4	<0.001
	No	44 (97.8%)	1 (2.2%)		

OR: Odds ratio, GCS: Glasgow Coma scale, ECG: Electrocardiogram, CBC: Complete blood count, ABG: Arterial blood gas, LFT: Liver function tests, HCO_3: Serum bicarbonates

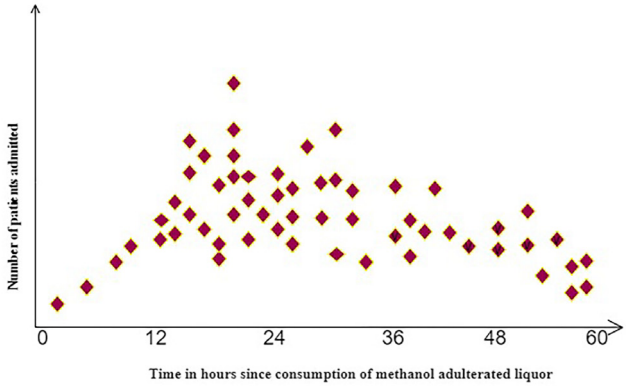

Figure 1. Patients' admission to hospital plotted against time since consumption of methanol adulterated liquor

The outbreak and its aftermath taught us many lessons and posed many questions. Ethanol intravenous preparations are not readily available, and their pharmacokinetics are erratic, with a risk of liver injury and hypoglycemia (13). Despite available resources for ethanol therapy, our patient population could not be motivated to accept it. Patients' and caregivers' reluctance to consent to ethanol treatment was rooted in social taboos and ill-founded misconceptions about further alcohol intake. The apprehension created by social and mass media, fueled the rejection of ethanol therapy. Fomepizole, on the other hand, was unattainable due to non-availability at regional pharmaceutical stores and financial and time constraints. Seven out of nine deaths occurred within 48 hours

of consumption, giving the administration hardly any time to mobilize fomepizole resources from nearby districts. Given this scenario, we were dependent on intensive monitoring and hemodialysis as the only means to salvage the situation. A review after the crisis period revealed salvage options like emergency purchase and expedited couriers from the nearest supply station/stockist, which could have averted delayed deaths.

The silver lining, however, was good triage and instantaneous support from the hemodialysis unit, which helped save lives. Sixteen patients underwent intermittent hemodialysis, among whom 3 died. The impact of hemodialysis in reducing mortality was not significant (p=0.08). Previous research work ascertains that hemodialysis never takes precedence in methanol poisoning in this era of ALD inhibitors, namely fomepizole and ethanol [3,10,11]. Nevertheless, it is an important salvage measure for patients with severe acidosis, acute kidney injury, and life-threatening dyselectrolytemias [6,10]. Chung et al. [14], in their case series, reported the non-disease-modifying effect of hemodialysis in methanol poisoning. In our experience, instituting intermittent hemodialysis, too, did not make a statistically significant difference in the outcome.

The mortality rate varies among developed and developing countries. In India, the experience from 2 tertiary centers documented a death rate between 7.5% and 10% [4,12]. Mortality at our institute fell beyond this range due to many reasons, foremost among them being the care team's limited experience and resource constraints. This was compounded by case flooding, rapid deterioration, ventilator shortage, and non-availability of fomepizole. According to previously published literature, a pH less than 7.22 was a specific predictor of mortality [15]. Another study identified depressed mentation and pH <7.00 to be associated with mortality [16]. The predictors of mortality in our series were depressed mentation, shock, and severe acidosis (pH: <7.2). Our findings mirror similar observations worldwide and thereby reiterate the importance of bedside clinical and point-of-care laboratory markers of prognosis [17].

In the future, the threat of such outbreaks looms large, possibly with more devastating consequences. Our only hope lies in pre-emptive readiness and standard institutional protocol. Though a meticulously structured protocol for such crises depends upon resources, expertise, and strategic location, we do have compelling evidence to recommend certain key elements in patient care. These are most applicable to semi-urban and rural tertiary care centers with limited resources.

1. Gastric decontamination is not effective in methanol poisoning because of rapid absorption [18]. Symptoms develop after a lag period of a few hours, thereby rendering activated charcoal ineffective. Moreover, methyl alcohol as such has limited binding capacity to charcoal [18].

2. Anticipation and activation of health care resources should be accomplished within a time frame of 12 hours from the presentation of the first few cases. A reliable estimation of the anticipated number of patients and peak hospitalization rate can be made with the help of public health authorities. In our series, 89.23% (58/65) of people who consumed the adulterated liquor developed symptoms. Among them, 86.21% were admitted within 48 hours, with admission rates peaking between 12 and 24 hours after consumption. 78% of deaths occurred within 48 hours.

3. Clinical triage tools include assessment of mental status, vital signs, and respiratory distress assessment by pulse oximetry and/or ABG analysis. In our series, we documented worse outcomes with depressed mentation (mortality 53.33%), shock (mortality 66.7%), and hyperpnea (mortality 55.56%).

4. A strong recommendation for ABG as the laboratory triage tool is made here. Serum formic acid level is an ideal investigation that might not be feasible in rural health centers.

5. Lastly, a minimum stock of fomepizole with adequate shelf life needs to be maintained at every such center. Lessons learnt the hard way taught us that ethanol might not be culturally acceptable to our patients/families in light of illiteracy and oversensitive media.

Study Limitations

The study has several limitations, most striking of which are its limited sample size and retrospective nature. Since patients were admitted at a wide range of time periods (6-60 hours) after consumption of adulterated liquor, data collection bias could not be avoided. Panic reactions in the affected population led to many unwarranted admissions, thereby diluting the specificity of clinical manifestations. Secondly, among patients presenting late with altered mentation and/or hemodynamic instability, early features of toxicity could not be reliably documented. Thirdly, a sizeable proportion of patients were referred from nearby primary care centers after initial stabilization. The effect of early resuscitation probably modified the clinical picture of these patients, which could not be ascertained due to the retrospective nature of the study. Fourthly, the mortality-reducing effect of fomepizole is proven beyond doubt in previous research studies [10,11,13]. Fomepizole was not used in our patients for the reasons mentioned above. As expected, we faced an inflated case fatality rate of 15.51%, well beyond the average in two previous outbreaks in India [4,12]. Therefore, in the absence of disease-modifying antidotes, the clinical and laboratory predictors of death lose their strength.

Conclusion

Methanol poisoning outbreaks will continue to occur for more reasons than one. Peak admission rates are to be anticipated at 12-24 hours post-consumption. Standard operating procedures need to be in place at all tertiary treatment centers duly overseen by public health authorities. Baseline triage tools include pH, mental status assessment, and hemodynamic instability. Every tertiary care hospital should maintain emergency reserves of fomepizole perennially and initiate treatment early in such cases based on pH <7.2, serum bicarbonates <10 mEq/L, and depressed mentation.

Ethics

Ethics Committee Approval: The study was approved by the Government Villupuram Medical College and Hospital Institutional Ethics Committee (approval number: GVMC/IEC/2023(2)/3, date: 12.12.2023).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: S.K., S.G., J.A., V.P.; Concept: S.K., S.G., Design: S.K., S.G., V.P.; Data Collection or Processing: J.A., V.P.; Analysis or Interpretation: J.A., V.P.; Literature Search: S.K., S.G., J.A.; Writing: S.K., J.A., V.P.

Conflict of Interest: No conflict of interest was declared by the authors.

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