ORIGINAL ARTICLE

STUDY OF ALTERATION IN COMMON LABORATORY PARAMETERS IN METHANOL POISONING CASES: LESSON LEARNED FROM THE HOOCH TRAGEDY IN AHMEDABAD, GUJARAT

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ABSTRACT

Introduction: Measurement of methanol in blood is important to confirm the diagnosis of methanol intoxication and can be valuable in assessing the response to treatment. However, blood methanol is measured using gas chromatography in specialty laboratories, and the measurement can take many hours to a few days to complete. Hence we tried to find surrogate makers of acute methanol poisoning that are easily available in most of the settings and any physician can treat such cases in tragic situations like that happened at this study centre.

Method: Retrospective cased based study of cases affected by hooch tragedy.

Results: RBS means, WBC, serum amylase, MCV value increased with increasing serum methanol level. However, they were not significantly related to serum methanol level(p values were 0.078, 0.125, 0.224, 0.08 respectively.) Mean of arterial blood bicarbonate levels was 12.3 ± 7.3 mmol/L, mean of arterial pH was 7.17 ± 0.22 and their levels were significantly related to serum methanol levels (p values 0.0231 and 0.012 respectively).

Conclusion: Among all the routinely done biochemical parameters, arterial bicarbonate level and pH significantly correlated with serum methanol level. And when methanol level is not available arterial pH and bicarbonate level can guide the therapy.

Keywords: Methanol Poisoning, biochemical parameter, pH

INTRODUCTION

Methanol (methyl alcohol or wood alcohol) is obtained from the destructive distillation of wood[1]. This distillation is accompanied by a distasteful smell that limits the palatability of methanol. With further distillation, the pure methanol is much more palatable and has many industrial and practical uses. The smallest amount of methanol reported to cause death is 15 ml of 40 percent methanol; the highest dose recorded for a survivor is in the range of 500 to 600 ml.[2,3] It is critical that a blood methanol level be determined as soon as possible if the diagnosis is suspected. If the clinical suspicion of methanol poisoning is high, treatment should not be delayed pending the reporting of a blood level. Methanol itself is essentially nontoxic[4]. It is metabolized by dehydrogenation to formaldehyde and then to formic acid. These two metabolites are highly reactive, readily bind to tissue proteins, and are known to interfere with oxidative metabolism through inhibition of the cytochrome oxidase system[5]. While most of the toxicity was previously attributed to

formaldehyde, it appears that formic acid is more likely responsible for these effects. Following ingestion, there is typically a lag period of about 12-24h before toxic manifestations occur. This interval can be quite variable, however, and ranges from less than one hour to over 72 h.[6] Lack of symptoms should therefore not be interpreted as indicating insignificant intoxication, particularly if the patient presents promptly following ingestion. The lag period is due to the slow conversion of methanol to formaldehyde.

The outbreak of methanol poisoning described in this paper occurred in Ahmedabad, Gujarat, India in July 2009. Most patients were received in three Municipal Corporation run tertiary care hospitals, Government hospital and few private/corporate setups. We, at the Shardaben Hospital (municipal corporation run hospital), received 178 patients in four days.

MATERIALS AND METHOD

Initial diagnosis was made based on a clinical history with sufficient evidence of intake of toxic alcohol, as well as the presence of high anion metabolic acidosis. The accidental exposure and amount of illicit liquors was confirmed by interviewing the patient, relatives and peripheral hospital workers. All patients were treated with cofactor therapy folinic acid (leucovorin) 50 mg IV every 6 h to accelerate formate metabolism. We administered supplemental thiamine (100 mg IV) and pyridoxine (50 mg IV) and methylcobalamin to all patients. Corticosteroid was also given to patients for visual changes in consultation with the ophthalmologists. All patients with a pH below 7.3 were treated with 1-2 meq/kg of sodium bicarbonate via IV bolus and volume expansion with isotonic saline to correct acidosis and promote diuresis. A maintenance infusion was then prepared by mixing approximately 133 meq of sodium bicarbonate in 1 L of D5W. The infusion rate was 150-250 mL/h. The appropriate rate was adjusted in individual patients according to the initial pH, fluid status and serum sodium level. The goal of treatment was maintenance of an arterial or venous pH above 7.35, at which point the infusion was discontinued.

As fomepizole was unavailable, patients were treated with ethanol (4-8 mL/kg of a 10% ethanol solution, followed by 0.5-1 mL/kg of 10% ethanol solution infused per h and 50 ml of 95% through Ryle's tube) in any patient with documented recent ingestion of methanol or strong clinical suspicion of ingestion of methanol with an arterial pH <7.3, bicarbonate <20 mEg/L, A standard protocol of therapy was initiated in all the patients to start with and was modified later according to individual patient's needs. Intervention as and when required done. But these management aspects are out of scope of this article.Data collection: relevant study data was taken from the cases afterwards and entered into the excel sheet in the prescribed manner.

Data was analysed using epi2000 software. Individual variables are compared using the Mann-Whitney/Wilcoxon Two-Sample Test (Kruskal-Wallis test for two groups). Values are expressed as mean±SD, and $P<0.05$ was considered to be statistically significant. Linear regression method was used to derive the cut-off values mention in the table.

RESULTS

Mean age of presentation was 41.9±10.2 years. Most of them were men (175 out of 178).From those patients were history was possible to elicit, it was found that the mean time of presentation was 30 h and few were carried in as lately as 100 h after history of ingestion. However, those who were brought in late (n=7) were relatively stable (normal vitals, no visual or neurological symptoms) and dropped in because of panic. Patients presented with breathlessness, visual symptoms, altered mental status. Hemoglobin was 10.2±1.1 mg%; mean base deficit was 18.4 mmol/L (range 2-29), anion gap of 25 mmol/L, serum osmolality was 325 mOsm per kg of

water. Analysis of urine showed a pH of 5.5 with no crystals evident. Mean serum methanol level was 87.1 mg/dL, the maximum was 376 mg/dL, the minimum was 12 mg/dL.

WBC counts were raised, ranged in between 7600 /dl-14200 /dl. S. SGPT level were 54-156 units. Blood urea nitrogen (BUN) was 12 mg/dl and creatinine 1.0 mg/dl. Leukocyte count was 7,000 per/dl. Mean of Serum amylase level was in between 30 and 384 mg%. mean value 124 mg%. Serum RBS level were increased in most of the patients, with mean value of 168 ± 32 mg %. Means of serum potassium level was 4.2 ± 2.1 mEq/dl. Mean of MCV was 92 ± 12 fl.

Mean of arterial blood bicarbonate levels was 12.3±7.3 mmol/L, mean of arterial pH was 7.17±0.22 and their levels were significantly related to serum methanol levels (p values 0.0231 and 0.012 respectively). When serum amylase level were correlated with serum methanol level, we found very weak association (p=0.432). Applying statistically test to find statistical correlation of methanol level with RBS level, Potassium level, WBC count and MCV; P values were 0.078, 0.125, 0.224, 0.062 respectively. Table 1.

Table 1: Blood profile of the patients

Parameter studied	Comparision with S. Menthol (P values)
Serum potassium level (>4.5 mEq/dl)	0.125
RBS (above 168 mg%)	0.078
WBC count (above 6800/dl)	0.724
MCV value (above 100 fl/dl)	0.062
Arterial bicarbonate level (12.3 mEq/dl)	0.012
Arterial pH value(<7.1)	0.032
Serum amylase level (>300 IU/l)	0.432

Legend: table showing 'p' values derived when each variable was compared with serum methanol level. (values derived from direct application of linear regression)

DISCUSSION

In our study we found that serum amylase levels were increased in patients with higher serum methanol level, however it was not statistically significant. This rise is due to higher amylase released from salivary glands in alcoholic patients. Few patients of methanol poisoning have presented with even hemorrhagic pancreatitis. However pancreatitis has also been implicated as a cause of the abdominal pain, since high levels of serum amylase activity have been detected in many cases and pancreatitis has been confirmed in autopsy studies. BUN, serum creatinine were raised. Their rise is overtly visible, but their rise was not statistically significant when compared with serum methanol level. the mechanism of nephrotoxicity are multifactorial. the role of direct factors remain highly speculative. possible injury to the tubular cells due to the osmotic effects of high blood methanol concentration and cytotoxic effects related to the possible formate actions on

proximal tubular cells. among indirect factors, hemolysis and myoglobinuria were frequntly observed.[8,9]

Random blood sugar was raised in many patients, however it was not statistically significant when compared to serum methanol levels. This observation was also found by many researchers[4]. We found raised MCV level. Many studies also have shown that increase in red blood cell size which correlates well with the severity of methanol poisoning.[4,7,11]

The decrease in plasma bicarbonate closely parallels the increase in plasma formate concentration in both animal models as well as in human methanol poisoning, indicating that most or all of the acidosis is accounted for by formic acid production. A concomitant element of lactic acidosis is present in some cases. This may be due to the increased redox state of body tissues (i.e., increased ratio of NADH to NAD +) secondary to the oxidation of methanol and formaldehyde (Fig. 1). The increased redox state forces conversion of pyruvate to lactate. In addition, formic acid can interfere with intracellular respiration[10], thereby promoting anaerobic metabolism and lactate formation. However, in many cases flank circulatory shock and/or seizures are likely the predominant causes of increased lactate production.[11]

LIMITATION OF THE STUDY

It was a single center study with male dominance, hence needs to be studied on difference population. Timing of presentation of victims and background were different, hence some confounding factors cannot be eliminated.

CONCLUSION

MCV, RBS and serum amylase level are raised in methanol intoxication. Arterial pH and bicarbonate level correlate very well with the serum methanol level. Hence, cases with higher anion gap , higher osmolar gap metabolic acidosis, with alteration in above parameters should strongly favour methanol intoxication and treatment should not be delayed in such cases. And when methanol level is not available arterial pH and bicarbonate level can guide the therapy.

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