

Metabolic acidosis complicating ingestion of disinfectant floor cleaner containing butoxyethanol

服下含有丁氧基乙醇的地板消毒清潔劑引致代謝性酸中毒

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Butoxyethanol intoxication has seldom been reported. We describe a case of ingestion of butoxyethanol-containing cleaner resulting in high anion gap metabolic acidosis, which resolved after treatment with ethanol and haemodialysis. The presentations and treatments of previous cases are highlighted. Discussion is centred on the toxicological pathway of butoxyethanol and the role of alcohol dehydrogenase inhibitor. (*Hong Kong j.emerg.med.* 2007;14:99-102)

丁氧基乙醇中毒很少有報導。我們描述一個服下含有丁氧基乙醇清潔劑的個案，引致高陰離子差的酸中毒，經乙醇及血液透析治療後消退。我們強調以往個案的徵狀及治療，並集中討論丁氧基乙醇中毒的途徑及醇脫氫酶抑制劑的角色。

Keywords: Ethanol, ethylene glycols, pyrazoles, renal dialysis

關鍵詞：乙醇、乙二醇、吡唑、腎透析

Case

A 34-year-old man presented with repeated vomiting to the emergency department in December 2005, after ingesting 700 ml disinfectant floor cleaner with pH 6 and unknown concentrations of butoxyethanol (ethylene glycol butyl ether), alkyl dimethyl benzyl ammonium chloride and nonoxynol. The vital signs on arrival were: Glasgow Coma Score 15/15, blood pressure 117/72 mmHg, pulse rate 103/min and respiratory rate 18/min. Chest X-ray and ECG studies were normal. His throat was congested but chest pain, abdominal pain, dyspnoea and stridor were absent.

He remained conscious after transferral to the Intensive Care Unit. Blood sampling at 2 hours post-ingestion revealed the following values: pH 7.2, HCO₃ 5.9 mmol/L, BE -19.6, pO₂ 13.57 kPa, pCO₂ 2.09 kPa, Na 140 mmol/L, K 3.2 mmol/L, urea 3.5 mmol/L, creatinine 88 umol/L, Cl 98 mmol/L, glucose 8 mmol/L, osmolar gap 53 mOsm/kg (calculated without knowing the presence of any blood ethanol), anion gap 39.3 mEq/L and haemoglobin 16.8 g/dL. One hundred ml of 8.4% sodium bicarbonate was then given intravenously. He was intubated for airway protection to facilitate administration of intravenous 10% ethanol which was initiated at 6 hours post-ingestion with 50 g loading followed by infusion of 20 g/h. The first blood ethanol level 20 minutes prior to ethanol therapy was 22 mmol/L but there was no definite history of alcohol ingestion. During the first 2 hours of ethanol infusion, the blood ethanol level was maintained between 32 and 33 mmol/L. A 4-hour haemodialysis was commenced at 9 hours post-ingestion. The 2-hour post-haemodialysis blood gas was normalised with pH 7.38, HCO₃ 24.1 mmol/L and BE -1.2. The ethanol infusion was terminated at

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22 hours post-ingestion. One hour later, another 4-hour haemodialysis was undertaken in the presence of normal blood gas, electrolytes and renal function. He was extubated at the end of the haemodialysis session.

On day 1 of admission, he received oral pyridoxine 100 mg and intramuscular thiamine 100 mg. The thiamine was continued at 50 mg daily via oral route for 5 days. Upper gastrointestinal endoscopy examination revealed oesophagitis and gastritis. His subsequent haemodynamic status, blood gas and renal function were normal and he was discharged after six days of hospitalisation.

Analysis of the urine showed the presence of butoxyacetic acid but ethylene glycol and glycolic acid were undetectable. Butoxyethanol, not ethylene glycol, was identified in the blood sample. Cleaner of the same brand was found by laboratory analysis to contain butoxyethanol and 0.4% ethanol but no ethylene glycol.

Discussion

The ingredients of the cleaner in our case consisted of alkyl dimethyl benzyl ammonium chloride, a cationic

detergent capable of causing local irritation and caustic burn, nonoxynol, an anionic detergent much less toxic than the cationic one, and butoxyethanol, which was responsible for the metabolic acidosis. Reports of human poisoning as a result of butoxyethanol ingestion are infrequent. Of the nine reported cases in Table 1, metabolic acidosis was the invariable complication. Impairment of consciousness and hypotension to different extents were usually encountered.¹⁻⁸ There was one case of death³ and one who recovered with choreoathetoid movement lasting for two months.⁵

In animal models, butoxyethanol is initially metabolised to butoxyacetaldehyde by alcohol dehydrogenase and then converted to butoxyacetic acid.^{9,10} In vitro and animal trials suggested that humans are relatively free from the haemolysis observed in animals as a result of conversion of butoxyethanol to butoxyacetic acid.¹¹⁻¹³ Clinically, there were three reports suggesting rather than concluding haemolysis.^{1,2,5} Although butoxyacetic acid-mediated haemolysis is not a major concern in human, the chemicals in the metabolic pathway of butoxyethanol leading to the multi-organ pathologies have not been clearly identified. It is possible that the acidosis resulting from butoxyacetic acid formation causes central nervous

Table 1. Summary of the case reports on butoxyethanol poisoning

Ref	Age	Dose	C	BP	Hb	Cr	HCO ₃	pH	AG	BAA	EG	OU	ET	P	HD	S
1	50	30-60 g	↓		9.7	↑	5	7.23				Y				Y
2	23	63.5 g	↓	80/?	8.9		2.4	7.08	27.8			N			Y	Y
3	87	6.5%	↓	↓		↑	↓	↓			1.77		Y		Y	N
4	53	45.5 g	↓	60/30		115	5.6	7.05					Y		Y	Y
5	19	150-315 g	↓	58/?			11	7.36		Y					Y	Y
6	52	13.7 g	↓			170		7.19	45		4.95	Y	Y	Y		Y
7	57	24-72 g	↓	91/54		71	12	7.31	15	Y			Y			Y
8	18	79.2-88 g	↓			137	4.3	7.34		Y	N		Y		Y	Y
9	18	105.6 g	Alert			115	19.3	7.4		Y	N		Y		Y	Y
Our case	30	700 ml	Alert	117/72	16.8	88	5.3	7.2	39.3	Y	N		Y	N	Y	Y

AG: anion gap (mEq/L); BAA: butoxyacetic acid detection; BP: blood pressure (mmHg); C: consciousness; Cr: creatinine (umol/L); EG: ethylene glycol detection in blood (mmol/L); ET: ethanol therapy; Hb: haemoglobin (g/dL); HCO₃: bicarbonate (mmol/L); HD: haemodialysis; N: No; OU: oxaluria detection; P: pyrazole therapy; Ref: reference; S: survival; Y: yes; ↓: decreased level or impaired; ↑: increased level; Empty box means data not presented or unavailable.

system depression, hypotension and other widespread damages. Thus alcohol dehydrogenase inhibitors such as pyrazole and ethanol should be considered in butoxyethanol ingestion or poisoning. The short elimination half life of butoxyethanol of 40 minutes would prompt their early administration.^{7,14} However, late ethanol administration was deemed justified in our patient who had significant baseline blood ethanol concentration, given the prolongation of butoxyethanol half life to 210 minutes in concomitant ethanol ingestion.² Despite the lack of detrimental effect of pyrazole on the survival of rats administered with butoxyethanol, there remains questions in human whether butoxyethanol itself is toxic or more toxic than its metabolites. If this assumption is true, administration of alcohol dehydrogenase inhibitors will not achieve the predicted therapeutic effect or will even pose greater and longer toxicity. Haemodialysis may be advantageous in avoiding any undesirable interaction between ethanol and butoxyethanol, for the reason of directly removing the butoxyethanol and its metabolites as well as correcting the acidosis and electrolyte abnormalities. Haemodialysis is considered effective for eliminating butoxyethanol and butoxyacetic acid because of their dialyzable properties.^{14,15} There were reports of haemodialysis hastening the elimination of butoxyacetic acid.^{2,8} In the cases in Table 1, more than half were treated with ethanol and haemodialysis and it appeared that the clinicians often favoured their combined use. Measurement of the blood levels of butoxyethanol and butoxyacetic acid before and after haemodialysis provides direct assessment of the efficacy and predicts subsequent need of haemodialysis but this assay is not widely available. In general, we consider acid-base and clinical response better guides to further haemodialysis than butoxyethanol or butoxyacetic acid level for which a correlation with toxicity is not yet known.

Animal data indicate that 10% of the butoxyethanol is excreted as ethylene glycol in urine.¹⁶ There were reports in human, arousing the consideration of metabolic conversion of butoxyethanol to ethylene glycol. Oxaluria up to 100 mg/g creatinine was present in one case.¹ Two cases had blood ethylene glycol of 1.77 and 4.95 mmol/L respectively.^{3,6} However, no detailed analysis of the products was mentioned in these three reports. Metabolism into ethylene glycol was

not evident in our case even after administration of ethanol. According to our opinion, the utilisation of alcohol dehydrogenase inhibitors in butoxyethanol poisoning should not be precluded for the fear of enhancing ethylene glycol formation because the production of toxic metabolites from ethylene glycol will be inhibited under a sufficient dose of alcohol dehydrogenase inhibitors. Figure 1 illustrates the metabolic pathway of butoxyethanol according to the evidence to date.^{1,16}

Conclusion

Ingestion of disinfectant cleaner containing butoxyethanol may produce local gastrointestinal injuries and systemic toxicities like acidosis. In human, butoxyethanol is metabolised to butoxyacetic acid and probably ethylene glycol. There may be a therapeutic role of alcohol dehydrogenase inhibitors for inhibiting the formation of toxic metabolites if given in time. Although data on the effect of haemodialysis on the toxicokinetics of butoxyethanol and its metabolites are limited, we found this treatment beneficial in our patient who had significant metabolic acidosis.

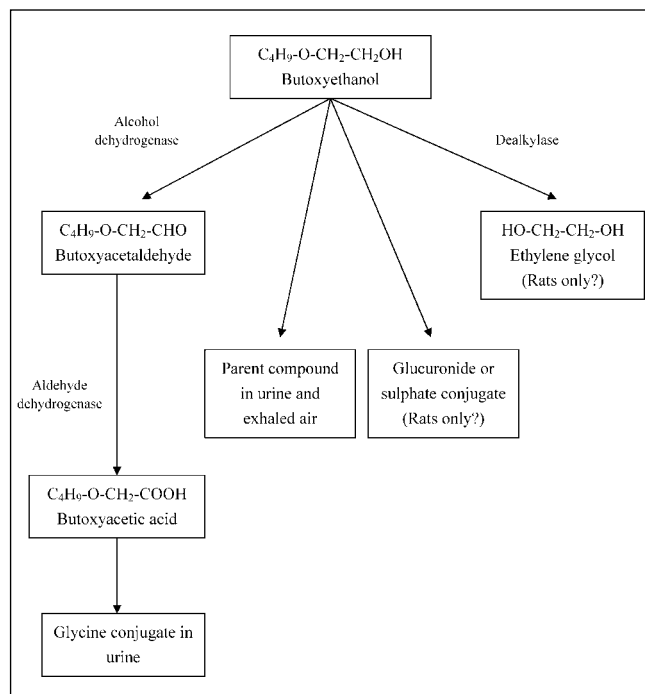


Figure 1. Metabolic pathway of butoxyethanol.

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