Acute Renal Failure following Accidental Potassium Bromate Poisoning: A Case Report

JAO Okeniyi*, TA Aladekomo**, OA Oyelami+

Summary

Okeniyi JAO, Aladekomo TA, Oyelami OA. Acute Renal Failure following Accidental Potassium Bromate Poisoning: A Case Report. Nigerian Journal of Paediatrics 2003; 30:150. Accidental poisoning is common in children. Potassium bromate is a commonly used additive and raising agent in many edibles particularly bread, a staple food worldwide, yet its accidental poisoning has hitherto, not been documented in Nigeria. We report an unusual case of acute renal failure following accidental ingestion of potassium bromate tablets.

Key Words: Acute renal failure, Poisoning, Potassium bromate

Introduction

POTASSIUM bromate (KBrO₃) is an oxidizing agent used not only as a food additive mainly in bread baking,¹ but also as a neutralizer in many hair curling kits.² It has been shown to cause severe and oftentimes, irreversible changes including carcinogenesis in experimental animals²⁻⁴ and humans.⁴⁻⁶ Accidental poisoning by various agents is well documented in children.⁷⁻⁹ This paper reports a case of potassium bromate ingestion by a child who subsequently developed acute renal failure (ARF). This report is believed to be the first of such in Nigeria.

Case report

AC, a 17 month-old girl, presented at the children's emergency room of the Wesley Guild Hospital, Ilesa, a unit of the Obafemi Awolowo University Teaching Hospitals Complex, on January 31, 2002. The initial complaints were vomiting, frequent and loose watery stools and weakness, all of a few hours' duration. She had been well until the day of presentation. Past medical history was not contributory. She was the only child

Obafemi Awolowo University Teaching Hospital (OAUTH), Ile-Ife

Wesley Guild Hospital, OAUTH Complex, Ilesa

* Senior Registrar

Department of Paediatrics and Child Health

** Lecturer

⁺ Associate Professor

of a 24-year old mother who was a petty trader, while her father was a 29-year old baker. On examination, she was fairly well nourished, weighing 9.2 kg with signs of some dehydration, mild pallor, watery rhinorrhoea and tipped hepatosplenomegaly. An initial assessment of gastroenteritis, probably of viral origin, with some dehydration was entertained. She received WHO oral rehydration salts solution (ORSS), but the diarrhoea and particularly the vomiting persisted; she was therefore commenced on intravenous Ringer's lactate with 50 percent dextrose augmentation. By 24 hours of admission, the diarrhoea and vomiting had subsided; she was well hydrated, ambulant and looked well. At this stage, she was reverted to oral rehydration therapy (ORT) and clinical observation for about 24 hours while awaiting discharge. The blood pressure and the haematocrit were not checked on admission. By 48 hours however, it was observed that she had not passed any urine despite good hydration. It was only at this stage that her mother volunteered the history of ingestion of at least, one tablet of potassium bromate (stored at their house for bread baking) about four hours before presentation, but that her mouth had been promptly rinsed with water. At 72 hours, and despite good hydration, she was still to pass any urine. A frusemide renal challenge was carried out, but a suprapubic needle aspiration yielded no urine. An assessment of ARF secondary to probable accidental potassium bromate poisoning was then made.

By the following day, she had developed facial puffiness and pedal oedema, her weight was 9.9 kg, blood pressure 140/90 mmHg, pulse rate 120 beats per minute and packed cell volume 26 percent. The serum electrolytes on days 4, 7 and 15 are shown in Table I. She could not be dialysed due to lack of facilities, but her fluid intake was restricted to 400 ml/ m²/24 hours. She was also commenced on multivitamins (including vitamin C), intravenous 10 percent calcium gluconate and sodium bicarbonate. On the evening of the fifth day, she wet her bed and by the seventh day, she was less puffy and weighed 9.7 kg. Between the eighth and 11th days, she had entered the polyuric phase of the ARF making between 390-420 ml of urine per 24 hours. Her blood pressure was now 100/50 mmHg. The urine dipstick investigation on the 11th day showed a pH of 6.8, with traces of ascorbic acid, red blood cells and protein (albumin). She was discharged on the 11th day at her mother's request. When she was seen in the clinic on the 15th day, she weighed 10 kg. Thereafter, she was lost to follow up.

Table I

Serum Electrolyte and Urea Levels in the Patient

	Day 4	Day 7	Day 15
Creatinine (imol/l)	660	550	154
Urea (mmol/l)	12.7	12.6	2.5
Sodium (mmol/1)	130	127	122
Potassium (mmol/l)	5.6	3.9	5.3
Bicarbonate (mmol/l)	15	25	18

Discussion

Accidental poisoning is very common in childhood,^{7, 8} mostly in those aged five years and below. It usually involves a single substance often commonly used at home, with ingestion being the most common route of exposure. Most cases are also manageable at home.⁹ This case fits the above scenario except that the poisoning was by potassium bromate, few cases of which have been reported before, ¹⁰ but none from Nigeria where its use is still commonplace and unregulated, despite the well orchestrated media reports against it.

Potassium bromate is an oxidizing agent¹¹ widely consumed in bread in which it is used as an additive in the baking process. It is also readily available in thioglycolate-containing hair-curling kits.² However in this case, it was ingested in the form of 60-ppm tablet (which is normally applied to 100 lbs of baking flour), which the patient's father, a baker, had stored at home. Following the accidental ingestion, he had only rinsed

the patient's mouth, gave corn flour cereal (pap) and thought no further of the incident. She presented with some known side effects of potassium bromate toxicity, which include vorniting, diarrhoea, renal damage with albuminuria and oliguria. Other known side effects include hypotension, pulmonary oedema, hepatitis and cardiac failure from toxic myocarditis. 12, 13 Fortunately, none of these other serious effects occurred in our patient. Even the acute renal failure was missed initially, hence the initial omission of urinalysis and monitoring of blood pressure.

Potassium bromate is particularly nephrotoxic.¹⁴ It is known that death from renal failure may occur in one to two weeks in rats. It is also carcinogenic in experimental animals14-16 and in human kidney tissue in vitro. 17,18 It has been shown to induce renal failure and irreversible sensorineural hearing loss in guinea pigs,2 testicular and peritoneal mesotheliomas in rats19 and immediate and delayed signs of vestibular dysfunction in dogs.⁵ The carcinogenic risks to humans have been evaluated4 and the WHO has recommended acceptable limits of daily intake.3 The compound in water concentration as low as 0.02 g/l (20 ppm: 1.5 mg/kg/day) has been documented to be carcinogenic in rodents.²⁰ However, reports suggest a lack of renal tumour-initiating activity of a single dose of 300mg/ kg of KBrO, 21 Our patient presumably consumed between 60-120 ppm with a body weight of less than 10kg equating to 4.5-9.0 mg/kg.

Various methods have been described for the determination of bromate residues with accuracy in a variety of baked goods.^{22, 23} The nephrotoxicity is thought to result from an interplay of increased formation of reactive oxygen species, 14,16,24 lipid peroxidation,25 induced DNA fragmentation,21,26 micronuclei formation, and induced cellular proliferation.^{11, 27} A clear sex difference has been reported in the susceptibility of rat kidney to the generation of the oxidative stress.26 Male rats show a rapid and persistent response as against an increase that only becomes apparent three weeks after exposure in the females; the significance of this to humans is not yet known. The antioxidants, ascorbic acid (vitamin C), vitamin E, cysteine and glutathione are the only substances documented to have potential against the carcinogenicity of KBrO, 15 Attempts have been made to find an acceptable substance for potassium bromate in the bread baking process. A Venezuelan study demonstrated the technical feasibility of replacing 80 ppm of KBrO, for 20 ppm of ascorbic acid in the flour, without affecting the bread acceptability.1

Due to its potential hazardous effects, potassium bromate has been banned in various countries. There is legislation against its use in the bread baking industry

in Nigeria, while the National Agency for Food and Drug Administration and Control had in the past, destroyed bread made with potassium bromate in some cities in the country. The legislation has however, not been widely enforced. As typified by this case, the average hospital in the country may be unable to cope with the effects of poisoning by such a lethal vet commonplace substance. Therefore, education on the prevention of poisoning by this substance should be carried out in places such as well child clinics and over the electronic media. Parents should be counselled about potential poisons and how to prevent access to them by for example, the use of child-resistant packaging of drugs and other pharmaceutical preparations. They should also be informed on what to do if poisoning occurs. This should diminish the likelihood of serious morbidity or mortality from such exposure.

Acknowledgements

We wish to thank the entire medical staff of the department of Paediatrics, Mr. Toluwase of the department of Chemical Pathology and Drs. Akintunde and Oyedeji, all of the Wesley Guild Hospital, Ilesa for their assistance.

References

- Corrales X, Guerra M, Granito M, Ferris J. [Substitution of ascorbic acid for potassium bromate in the making of French bread.] [Spanish] Archivos latinoamericanos de Nutricion 1993; 43: 234-40.
- Chuu JJ, Hsu CJ, Lin-Shiau SY. The detrimental effects of potassium bromate and thioglycolate on auditory brainstem response in guinea pigs. *Chin J Physiol* 2000; 43: 91-6.
- 3. Anonymous. Evaluation of certain food additives and contaminants. WHO Tech Rep Ser 1995; 859: 1-54.
- Anonymous. Potassium bromate. IARC Monographs on the evaluation of carcinogenic risks to humans 1999; 73: 481-96.
- Gayer PT. Toxic mechanism of bromate poisoning in a dog: a case study. Vet Hum Toxicol 1994; 36: 208-11.
- Murata M, Bansho Y, Inoue S, Ito K, Ohnishi S, Midorikawa K, Kawanishi S. Requirement of glutathione and cysteine in guanine-specific oxidation of DNA by carcinogenic potassium bromate. *Chem Res Toxical* 2001; 14: 678-85.
- Matthews TS. Poisoning in childhood. In: Hendrickse RG, Barr DGD, Matthews TS, eds. Paediatrics in the Tropics 1st ed., Oxford: Blackwell Scientific Publications. 1990; 876-81.

- Sibert JR, Davies PA. Poisoning, Accidents and Sudden Infant Death Syndrome. In: Campbell AGM, McIntosh N, eds. Forfar and Arneil's Textbook of Paediatrics. Edinburgh: Churchill Livingstone, 1994: 781-806.
- Rodgers GC Jr, Matyunas NJ. Poisonings: Drugs, Chemicals and Plants. In: Behrman RE, Kliegman RM, Jenson HB, eds. Nelson Textbook of Pediatrics 16th ed Asia, WB Saunders Harcourt 2000; 2160-70.
- 10. De Vriese A, Vanholder R, Lameire N. Severe acute renal failure due to bromate intoxication: report of a case and discussion of management guidelines based on a review of the literature. Nephrol Dial Transplant 1997; 12: 204-9.
- 11. Umemura T, Sai K, Takagi A, Hasegawa R, Kurokawa Y. A possible role for oxidative stress in potassium bromate (KB10₃) carcinogenesis. *Carcinogenesis* 1995; 16: 593-7.
- 12.Ballmaier D, Epe B. Oxidative DNA damage induced by potassium bromate under cell-free conditions and in mammalian cells. *Carcinogenesis* 1995; 16: 335-42.
- 13.Umemura T, Kodama Y, Kurokawa Y, Williams GM. Lack of oxidative DNA damage or initiation of carcinogenesis in the kidneys of F344 rats given subchronic exposure to p-dichlorobenzene (pDCB) at a carcinogenic dose. *Arch Toxicol* 2000; **74**: 54-9.
- 14.Sai K, Uchiyama S, Ohno Y, Hasegawa R, Kurokawa Y. Generation of active oxygen species in vitro by the interaction of potassium bromate with rat kidney cell. Carcinogenesis 1992; 13: 333-9.
- 15.Sai K, Hayashi M, Takagi A, Hasegawa R, Sofuni T, Kurokawa Y. Effects of antioxidants on induction of microfiuclei in rat peripheral blood reticulocytes by potassium bromate. *Muta Res* 1992; 269: 113-8.
- 16.Cho DH, Hong JT, Chin K, Cho TS, Lee BM. Organotropic formation and disappearance of 8hydroxydeoxyguanosine in the kidney of Sprague-Dawley rats exposed to adriamycin and KBrO₃. Cancer Lett 1993; 74: 141-5.
- 17. Robbiano L, Carrozzino R, Puglia CP, Corbu C, Brambilla G. Correlation between induction of DNA fragmentation and micronuclei formation in kidney cells from rats and humans and tissue-specific carcinogenic activity. *Taxicol Appl Pharmacol* 1999; 161: 153-9.
- 18. Murata M, Bansho Y, Inoue S, Ito K, Ohnishi S, Midorikawa K, Kawanishi S. Requirement of glutathione and cysteine in guanine specific oxidation of DNA by carcinogenic potassium bromate. Chem Res Toxical 2001; 14: 678-85.
- 19. Crosby LM, Morgan KT, Gaskill B, Wolf DC, De Angelo AB. Origin and distribution of potassium bromate-induced testicular and peritoneal mesotheliomas in rats. Taxicol Pathol 2000; 28: 253-66.

- 20.DeAngelo AB, George MH, Kilburn SR, Moore TM, Wolf DC. Carcinogenicity of potassium bromate administered in the drinking water to male B6C3F1 mice and F344/N rats. Toxical Pathol 1998; 26: 587-94.
- 21. Kurata Y, Diwan BA, Waro JM. Lack of renal tumourinitiating activity of a single dose of potassium bromate, a genotoxic renal carcinogen in male F 344/ NCr rats. Food Chem Toxicol 1992; 30: 251-9.
- 22. Dennis MJ, Burrell A, Mathieson K, Willetts P, Massey RC. The determination of the flour improver potassium bromate in bread by gas chromatographic and ICP-MS methods. *Food Addit and Contam* 1994; 11: 633-9.
- 23.Himata K, Noda M, Ando S, Yamada Y. Measurement of bromate in bread by liquid chromatography with postcolumn flow reactor detection. J AOAC Int 2000; 83: 347-55.
- 24.Loft S, Deng XS, Tuo J, Wellejus A, Sorensen M, Poulsen HE. Experimental study of oxidative DNA damage

- [Review]. Free Radic Res 1998; 29: 525-39.
- 25.Sai K, Tyson CA, Thomas DW. Dabbs JE, Hasegawa R, Kurokawa Y. Oxidative DNA damage induced by potassium bromate in isolated rat renal proximal tubules and renal nuclei. Cancer Lett 1994; 87: 1-7.
- 26.McLaren J, Boulikas T, Vamvakas S. Induction of poly(ADP-ribosyl)ation in the kidney after in vivo application of renal carcinogens. *Taxicology* 1994; 88: 101-12.
- 27. Umemura T, Sai K, Takagi A, Hasegawa R, Kurokawa Y. A possible role for cell proliferation in potassium bromate (KBrO₃) carcinogenesis. J Cancer Res Clin Oncol 1993; 119: 463-9.
- 28. Umemura T, Takagi A, Sai K, Hasegawa R, Kurokawa Y. Oxidative DNA damage and cell proliferation in the kidneys of male and female rats during 13-weeks exposure to potassium bromate (KBrO₃). Arch Taxicol 1998; 72: 264-9.