SHORT REPORTS

Mortality in sodium chlorate poisoning

Sodium chlorate poisoning is rare but is associated with a high mortality rate,¹ death occurring from massive intravascular haemolysis and acute renal failure. We report the outcome in 14 patients poisoned by sodium chlorate, with special regard to the amount ingested and subsequent management.

Patients, treatment, and results

During 1974-8 we followed up in detail 14 cases of sodium chlorate poisoning referred to the National Poisons Information Service (Guy's Hospital). Data concerning the amount of substance ingested, medical management, and subsequent outcome were obtained (see table). Mortality was high (64%), and death invariably occurred, irrespective of treatment, when the amount of sodium chlorate ingested exceeded 100 g. Early deaths—that is, those within 24 hours—were more common in accidental self-poisoning, when specific antidotes or reducing agents were not administered owing to the delay in diagnosis. Supportive management alone was successful in only one patient (case 12); in this case the ingested amount was less than one-tenth of the stated fatal dose of 20-30 g. In the four other survivors recovery was associated with ingested amounts of 100 g or less of sodium chlorate, prompt administration of sodium thiosulphate or reducing agents, and management of acute renal failure by peritoneal dialysis or haemodialysis. The success of treatment with specific antidotes followed by dialysis is best seen by comparing cases 1 and 14, in which the amounts of sodium chlorate ingested were identical. The clinical features of sodium chlorate poisoning occurred in the following frequency: nausea and vomiting (11 patients; 79%), cyanosis (seven; 50%), abdominal pain (five; 36%), diarrhoea (three; 21%) and dyspnoea (three; 21%). Two patients were admitted in coma and died shortly afterwards. Seven patients became anuric within 48 hours after admission to hospital. Methaemoglobinaemia was found in 13 patients, in two of whom peripheral blood films showed the presence of ghost cells and Heinz-body formation. In the patients who died a constant necropsy finding was a "chocolate" discoloration of the blood and viscera due to staining by bilirubin and methaemoglobin.

Comment

Sodium chlorate is a powerful oxidant used extensively as a herbicide. A white crystalline substance, it is applied dissolved in water. The crystals may be mistaken for sugar with fatal results (cases 3 and 8). Poisoning usually results from ingestion but has been reported after inhalation of atomised droplets.² Initial symptoms relate to the irritant effect of the chlorate ion on the gastrointestinal mucosa. After absorption haemoglobin is rapidly oxidised to methaemoglobin and intravascular haemolysis results. Cyanosis becomes clinically detectable when the proportion of methaemoglobin exceeds 10%; values above 70% are fatal. Death occurring within a few hours of ingestion is attributed to tissue hypoxia due to severe methaemoglobinaemia or hyperkalaemia resulting from massive haemolysis. Sodium chlorate is nephrotoxic and causes acute tubular necrosis; the ensuing renal failure may be compounded by haemoglobinuria.

In cases presenting early initial management should comprise gastric lavage and administration of activated charcoal. Sodium thiosulphate (2-5 g in 200 ml of 5% sodium bicarbonate) is a specific

antidote that inactivates the chlorate ion and may be given by mouth or intravenously. Methaemoglobinaemia is best treated by giving intravenous methylene blue (20-50 ml of a 1% solution), which is superior to ascorbic acid in reducing methaemoglobin to haemoglobin.³ Oxygen is of no value. Sodium chlorate is freely dialysable, and early treatment of renal failure by peritoneal dialysis or haemodialysis is recommended. Despite isolated reports of success in treating severe sodium chlorate poisoning,^{4,5} the mortality rate remains extremely high. Sodium chlorate is freely available and is not listed as a poison: preparations of it are therefore not required to carry any warning to this effect.

¹ Dérot, M, *et al*, *Semaine des Hôpitaux de Paris*, 1948, **24**, 719.

² Jackson, R C, Elder, W J, and McDonnell, H, *Lancet*, 1961, **2**, 1381.

³ Jaffé, E R, and Newmann, G, *Nature*, 1962, **202**, 607.

⁴ Knight, R K, Trounce, J R, and Cameron, J S, *British Medical Journal*, 1967, **3**, 601.

⁵ Lee, D B, *et al*, *British Medical Journal*, 1970, **2**, 31.

(Accepted 27 February 1979)

Poisons Unit, New Cross Hospital, London SE14 5ER

M HELLIWELL, MB, MRCP, registrar in intensive care and clinical toxicology
J NUNN, BSc, information officer

Painful gynaecomastia treated with tamoxifen

Unilateral or bilateral gynaecomastia may be a consequence of impaired liver function or lung cancer or occur after certain drugs, notably digoxin, spironolactone, metoclopramide, and cimetidine. In lung cancer gynaecomastia is associated with gonadotrophin-secreting tumours, and there is also an association with hypertrophic pulmonary osteoarthropathy.¹ Histologically the tumour is usually anaplastic large-cell carcinoma, but there are reported cases with squamous-cell carcinoma, adenocarcinoma, and oat-cell carcinoma.² Gynaecomastia is usually no more than embarrassing for the patient, but rarely it may be painful. This was the case in the three patients described below. The oestrogen antagonist tamoxifen successfully relieved the pain.

Case reports

Case 1—A 64-year-old heavy smoker presented with weight loss and non-productive cough. Chest radiography showed a right upper lobe opacity with extensive hilar enlargement. Sputum cytology disclosed an oat-cell carcinoma of the bronchus. On presentation he had bilateral gynaecomastia of recent onset. Biochemical liver function values and a liver scan were normal. The gynaecomastia progressed and became intensely painful with little relief from analgesics. Liver function values were abnormal and the serum oestradiol concentration was 455 pmol/l (124 pg/ml) (normal range 55-147 pmol/l; 15-40 pg/ml). He was given tamoxifen 10 mg twice daily. The gynaecomastia regressed and became painless in two weeks. He

Details of 14 cases of sodium chlorate poisoning showing management and outcome

Case No	Age	Sex	Amount ingested	Deliberate or accidental	Initial management	Further management	Outcome
1	55	F	100 g	Deliberate		Supportive	Died (3 hours)
2	55	M	150 g	"	Methylene blue, ascorbic acid	Mannitol hydrocortisone	Died (36 hours)
3	3	M	Unknown	Accidental	"	Supportive	Died (6 hours)
4	23	M	100-150 g	Deliberate	Sodium thiosulphate, ascorbic acid	Blood transfusion, hydrocortisone, antibiotics	Died (48 hours)
5		F	30 g	"	Methylene blue, ascorbic acid	Peritoneal dialysis, blood transfusion	Died* (5 days)
6	25	M	50 g	"	Methylene blue	Haemodialysis, exchange transfusion	Died† (5 hours)
7	28	M	300 g	"	Methylene blue	Peritoneal dialysis, exchange transfusion	Died
8	46	F	15 g	Accidental		Supportive	Died (20 hours)
9	48	M	Unknown	Deliberate	Methylene blue, ascorbic acid	Supportive	Died‡ (2 hours)
10		F	45 g	"	Sodium thiosulphate	Peritoneal dialysis	Recovered
11	18	F	30 g	"	Sodium thiosulphate, methylene blue	Peritoneal dialysis	Recovered
12	47	M	1-2 g	Accidental	Sodium thiosulphate	Supportive	Recovered
13	13	M	5 g	"		Peritoneal dialysis, blood transfusion	Recovered
14	18	F	100 g	Deliberate	Methylene blue, sodium bicarbonate	Exchange transfusion, haemodialysis	Recovered

*Necropsy showed portal vein thrombosis. †Fatal cardiac arrest during dialysis. ‡Severe hyperkalaemia present.

died six months later with no further pain and without recurrence of the gynaecomastia, the tamoxifen having been stopped after two months.

Case 2—A 67-year-old smoker was treated with radiotherapy to an inoperable squamous-cell carcinoma of the bronchus. Four months later he complained of painful, bilateral, asymmetrical gynaecomastia and wrist pain. Radiographs of the wrists were suggestive but not diagnostic of hypertrophic pulmonary osteoarthropathy. The breast and wrist pain disappeared within two weeks after starting tamoxifen, which was continued for a further three months. He died seven months later with no further symptoms from gynaecomastia or his wrists.

Case 3—This man, aged 73, had a long history of ischaemic heart disease with biventricular failure. He had received digoxin, spironolactone, and frusemide for several years, and when seen he had painful bilateral gynaecomastia. The digoxin and spironolactone were discontinued with no relief of pain. A biopsy specimen showed normal breast tissue. Analgesics were given for two months, with no relief. Tamoxifen was then begun and produced complete relief of pain within one week. Tamoxifen was stopped after six weeks with no recurrence of pain. The treatment caused no appreciable problems of fluid retention in this patient.

Comment

Tamoxifen produced regression of painless gynaecomastia in one other case of a gonadotrophin-secreting oat-cell carcinoma of the bronchus.³ In the present three cases tamoxifen produced relief from disablingly painful gynaecomastia and regression of the swelling, which was maintained when tamoxifen was stopped.

Digoxin and spironolactone bind to the oestrogen receptor and stimulate breast proliferation. Discussion continues on whether lung tumours produce oestrogens in addition to gonadotrophins.⁴ Nevertheless, in both cases tamoxifen could produce regression of gynaecomastia by blocking the oestrogen receptor. In case 2 the symptoms and signs suggestive of hypertrophic pulmonary osteoarthropathy, which has a known occasional association with gynaecomastia, were also relieved by tamoxifen. It has been suggested that the common link is altered oestrogen metabolism, and, if so, tamoxifen might relieve pain and be of benefit in pulmonary osteoarthropathy. From the three cases reported tamoxifen is certainly of benefit in painful gynaecomastia and deserves further study in treating pulmonary osteoarthropathy.

I am grateful for the advice of Professor M H Lessof.

¹ Fusco, F D, and Rosen, S W, *New England Journal of Medicine*, 1966, **275**, 507.

² Cottrell, J C, et al, *American Journal of Clinical Pathology*, 1969, **52**, 720.

³ Farilamb, D, and Boesen, E, *Postgraduate Medical Journal*, 1977, **53**, 269.

⁴ Kirschner, M A, Cohen, F B, and Jespersen, D, *Journal of Clinical Endocrinology and Metabolism*, 1974, **29**, 112.

(Accepted 16 February 1979)

Department of Medicine, Guy's Hospital, London SE1 9RT
D B JEFFERYS, BSC, MRCP, junior lecturer

Cytomegalovirus infection associated with lower urinary tract symptoms

Three members of a renal unit had a similar complex of urinary tract symptoms. Cytomegalovirus (CMV) was recovered from the urine of all three. Antibody titres against CMV during or shortly after the acute phase were negative, subsequently rising in two.

Case reports

All subjects were men over 30 years of age with no previous urological disorders. No subject's urine contained excess leucocytes, red cells, or protein. Cultures were bacteriologically sterile.

Case 1—This man had urgency and frequency of micturition, mild dysuria, suprapubic pain, nocturia, and the sensation of incomplete voiding. Symptoms developed over two days and lasted three weeks. After the initial illness an intravenous urogram was performed under steroid cover, and symptoms returned. Eight weeks later, alerted by the onset of similar symptoms in colleagues, urine was cultured for viruses and CMV isolated. CMV antibody could not be detected, but four weeks later was present at a dilution of 1/64.

Case 2—This man had an identical illness of similar duration. Four weeks afterwards, when asymptomatic, urine virus culture produced CMV. Antibody could not be detected either initially or one month later.

Case 3—He was on holiday during his colleagues' illnesses, and presented two weeks after returning. After a mild prodrome of malaise, headache, and myalgia he developed symptoms similar to the others, though dysuria was more severe. CMV was isolated from urine during the illness and eight weeks later. CMV antibody titre in the acute phase was less than 1/8, rising to 1/64 after 10 weeks.

All subjects agreed that the most striking feature was the sensation that voiding was incomplete. None had urethral discharge. Apart from the transient prodrome in case 3, no features of "classical" CMV infection were recognised. Coincident with their acute illnesses, the wives of two of the men (cases 2 and 3) had transient dysuria and frequency of micturition. The two young children of one of the men (case 3) had acute, non-suppurative parotitis for three days and malaise, fever, lymphadenopathy, hepatosplenomegaly, and generalised macular rash for five days, respectively. Neither underwent investigation. The subjects could not identify a single infective source, though all routinely handle urine and blood specimens, including those from patients receiving immunosuppressive treatment.

Virus studies—Freshly voided urine samples were neutralised and inoculated into human embryonic lung monolayer cultures. Isolates were identified by cytopathogenic effect and specific immunofluorescence. Antibody tests were by complement fixation using cytomegalovirus strain AD 169.

Comment

Attempts to identify CMV as an agent in non-specific urethritis have been unsuccessful.¹ Although dysuria may occur during a glandular fever-like illness due to CMV,² we know of no other report in which symptoms referable exclusively to the lower urinary tract have been associated with CMV isolation. The incidence of urinary excretion of CMV is high in patients receiving immunosuppressive treatment, and in one of our subjects (case 1) symptoms returned after administration of steroids. Other viruses have been associated with lower urinary tract disorders, including adenoviruses in acute haemorrhagic cystitis³ and *Herpesvirus hominis* type 2 in vulvovaginitis and penile infections.⁵

A fortuitous association between isolation of CMV in all and a rise of antibody titre in two of the three apparently non-immune subjects with identical clinical features is improbable. The unlikely possibility remains that another agent was responsible for the syndrome and reactivation of latent CMV had occurred. If the subjects had not worked in a renal unit their common illness may not have been recognised. This report shows the value of virus studies in patients with lower urinary tract symptoms without bacteriuria.

¹ Holmes, K K, et al, *New England Journal of Medicine*, 1975, **292**, 1199.

² Klenda, E, and Kääriäinen, L, *British Medical Journal*, 1965, **2**, 1099.

³ Mutson, M A, et al, *American Journal of Disease in Children*, 1971, **121**, 281.

⁴ Numazaki, Y, et al, *New England Journal of Medicine*, 1973, **289**, 344.

⁵ Nahmias, A J, and Roizman, B, *New England Journal of Medicine*, 1973, **289**, 781.

(Accepted 21 February 1979)

Department of Nephrology, The Children's Hospital, Birmingham
B16 8ET

J G DAVIES, MRCP, DCH, senior registrar

C M TAYLOR, MRCP, DCH, research fellow

R H R WHITE, MD, FRCP, consultant paediatrician and nephrologist

Department of Microbiology, The Children's Hospital, Birmingham,
B16 8ET

R H GEORGE, MB, MRCPATH, consultant microbiologist

D R PURDHAM, FIMLS, senior chief medical laboratory scientific officer

Controlled trial of cyclophosphamide in active chronic hepatitis

Although survival in hepatitis-B-negative active chronic hepatitis (ACH) is prolonged by corticosteroid treatment,¹ side effects are common,² so other effective treatments are needed. Azathioprine may be beneficial when combined with prednisone, although not when given alone.¹ Cyclophosphamide has been reported to induce biochemical remission of ACH³ and, in combination with prednisone, to produce dramatic histological resolution,⁴ but these observations