Three cases of fatal triazolam poisoning

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Triazolam, which is widely prescribed as a hypnotic, is considered to be safe even in overdose. In elderly patients, however, overdose may be fatal, particularly in patients taking concomitant drug treatment or with serious disease.

Case reports

Case 1—A 76 year old woman with bone pain from osteomalacia due to renal tubular acidosis had been treated with alfacalcidol, calcium supplements, sodium bicarbonate, and dihydrocodeine; she was receiving triazolam 0.25 mg as a hypnotic. She was found dead with a note indicating her intention to take her life. Her bottle of triazolam tablets was empty, but she had not taken an overdose of the other drugs. Necropsy showed early pneumonia and chronic bowel obstruction; these lesions were considered to be capable of having caused her death. In view of the suicide note samples were referred for toxicological analysis. This showed a blood triazolam concentration of 47 nmol/l, which is substantially above mean peak therapeutic concentrations.^{1,3} The equivalent of at least five tablets was found in the stomach. Dihydrocodeine was found in therapeutic concentration; analysis for other drugs yielded negative results.

Case 2—A 59 year old depressed woman had spoken frequently of suicide. A year before her death she had been prescribed triazolam several times; three days before her death she showed someone a hoard of tablets and spoke of taking her life. She was found dead with a partly consumed bottle of whisky. Necropsy did not show any anatomical lesions that might have accounted for her death. Toxicological analysis showed a blood triazolam concentration of 58 nmol/l and temazepam concentration of 3 µmol/l (the upper end of the therapeutic range).⁴ Small quantities of both drugs were found in her stomach. Her blood alcohol concentration was 45 mmol/l and urine alcohol concentration 18 mmol. Tests for other drugs yielded negative results.

Case 3—A 75 year old woman with schizophrenia and depression had been admitted to hospital several times after drug overdoses and had tried to slash her wrists. She was being treated by depot haloperidol injections monthly and was taking orphenadrine 50 mg

twice daily and triazolam 0.5 mg at night. She was found dead with two empty bottles of triazolam tablets beside her. Three days before her death she had acquired two prescriptions, each for 60 tablets of 0.25 mg triazolam. Necropsy showed severe degenerative narrowing of coronary arteries and other changes due to aging. Her blood triazolam concentration was 76 mmol/l, and the orphenadrine concentration was within the therapeutic range. Tests for other drugs yielded negative results.

Comment

Two of these patients had natural diseases that might have been responsible for their deaths; the third patient had taken a fairly high dose of temazepam and a considerable volume of alcohol. The circumstances of the deaths nevertheless indicated the possibility of self poisoning, making toxicological examination mandatory. The analyses indicated substantial overdose with triazolam in all three cases, and we concluded that triazolam poisoning was probably the main cause of death in these debilitated patients.

In a recent search of published reports we failed to find any case in which death was attributed principally to triazolam poisoning, implying that the drug is fairly safe when taken in excess; this may be true in young healthy people. The drug is difficult to measure in small amounts, and this may have led to triazolam poisoning being missed in patients with serious diseases or other intoxications. The techniques of measurement used in our cases will be described elsewhere.

The hazards of overdose led to barbiturates being replaced as hypnotics by drugs such as triazolam. Our recent experience indicates that patients who have taken triazolam should be monitored closely as this drug may not be as safe as is commonly supposed when taken in overdose by debilitated elderly patients.

We thank Mr W Duffy, the coroner of Gateshead Metropolitan Borough, for his permission to report these cases and Mrs D Scorer for secretarial help.

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Adverse consequences arising from misdiagnosis of food allergy

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Food allergy is rare,¹ but there is widespread belief that sensitivity to specific foods is a common cause of a variety of symptoms.² This belief is supported by publications in the popular press and by enthusiastic "alternative" practitioners, who may be medically qualified.

We report on four cases seen recently in this area in which the diagnosis of food allergy and treatment by a practitioner of alternative medicine delayed the diagnosis and treatment of serious organic disease.

Case reports

Case 1—A 43 year old man presented with symptomatic anaemia to a practitioner of alternative medicine, who diagnosed allergy to gluten, milk, and caffeine. Symptoms continued despite changes in the diet, and six months later he was referred by his general practitioner. On examination he was found to be anaemic, but there were no other specific findings. Investigation showed haemoglobin 74 g/l and faecal occult blood; gastroscopy and duodenal biopsy yielded normal results; and colonoscopy showed an annular carcinoma of midtransverse colon. A laparotomy was performed. There were hepatic metastases and the patient died 12 months after resection of the primary tumour.

Case 2—A 23 year old woman presented with a six month history of abdominal pain, weight loss, and diarrhoea with intermittent blood and mucus. Milk

allergy was diagnosed by a practitioner of alternative medicine, and her symptoms improved transiently when milk was withdrawn from her diet. She was referred six weeks later with recurrent symptoms. Physical examination yielded no unusual results. Sigmoidoscopy showed the characteristic appearances of Crohn's disease of the rectum, confirmed on biopsy. Her symptoms resolved quickly after treatment with sulphasalazine and she remained well.

Case 3—A 57 year old woman developed symptoms of weight loss, easy fatigue, and diarrhoea. She presented to a practitioner of alternative medicine, who diagnosed diabetes mellitus and intestinal candidiasis in addition to an allergy to gluten, milk, and other dietary constituents. No tests were performed on blood or urine, and the diagnosis was based on the "vegetest" in which the subject holds wires connected to a galvanometer adjacent to the suspect food and the electrical response is recorded. Her weight loss continued and she was referred by her general practitioner. Investigations included a duodenal biopsy, which showed subtotal villous atrophy. After treatment with a gluten free diet the appearances of her small bowel biopsy specimens improved, she gained weight, and she remained well on a gluten free diet.

Case 4—In 1981 a 13 year old girl was diagnosed as having anorexia nervosa but declined follow up and treatment. She continued to follow a highly restrictive diet until 1985, when she was seen by a food allergist who diagnosed multiple food hypersensitivity and prescribed an even more restricted diet together with a course of "enzyme potentiated desensitisation," but during this she was admitted to hospital after collapsing at home. She weighed 22 kg and was hypothermic, unconscious, with bradycardia at 40 beats/min and unrecordable blood pressure. A chest radiograph showed bronchopneumonia. She improved with

general supportive measures and regained consciousness. Both the patient and her mother were very resistant to any nutritional support and refused any form of food unless this was discussed with the food allergist whom she had consulted before. The patient died five days after admission. The cause of death was bronchopneumonia due to anorexia nervosa.

Comment

Patients with a variety of symptoms often present to practitioners of alternative medicine and it is likely that food allergy will be diagnosed on the basis of invalid investigations. Many of these patients have functional disorders, such as irritable bowel syndrome, depression, or hyperventilation,⁴ and nutritional deficiencies may result from treatment.⁵ More importantly, incorrect diagnosis and treatment may delay the diagnosis of serious organic disease such as colonic neoplasia, coeliac disease, inflammatory bowel disease, or anorexia nervosa until the disease is advanced, and in two of the patients reported on here this led to death.

Doctors need to be aware that the diagnosis of food allergy is usually incorrect and may obscure readily treatable but potentially lethal conventional diseases.

We thank Dr C A Loehry for permission to report case 4.

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Arterial oxygen tension and saturation in hospital patients: effect of age and activity

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Blood gas concentrations are the result of anatomical, physiological, and physical variables, which are usually age dependent.¹

About 30 000 blood gas analyses are performed each year in a 500 bed hospital.² Owing to the increasing number of elderly patients true reference values related to age would be helpful, but no conclusive studies have been published. Sorbini *et al* showed a linear relation between oxygen tension and age,³ but the numbers of patients aged over 60 in that and other studies were small.³⁻⁵

We therefore performed a study to (a) define reference values for oxygen tension and haemoglobin saturation related to age in an inpatient population with a high proportion of elderly people; (b) investigate the effect of bed rest and normal activity on these values; and (c) compare the clinical usefulness of oxygen tension and oxygen saturation measurements.

Patients, methods, and results

One hundred and eight patients aged 20 to 90 were studied out of 532 consecutive patients admitted for elective surgery. Patients were excluded because of overt cardiac, pulmonary, or metabolic disease; obesity (Quetelet index >25); or smoking (>10

cigarettes/day). Findings on preoperative assessment, including an electrocardiogram, a chest radiograph, and haematological and biochemical profiles, had to be normal. We obtained informed consent from 117 of 162 suitable patients. After testing six were excluded because of hyperventilation (pH >7.50, carbon dioxide tension <4.20 kPa) and three because of incomplete data. Blood gas analyses were performed twice. One value was obtained after at least 30 minutes' bed rest and the second value after activity, defined as a walk of at least 100 metres. Brachial or radial arterial blood samples were obtained from the patients in a semirecumbent position with a disposable, pre-heparinised system with a 22 gauge needle (Concord Micropulse). The samples were measured in duplicate within 10 minutes with an ABL-3 blood gas analyser (Radiometer) and a 282-CO oximeter (Instrumentation Laboratory).

Mean arterial oxygen tension differed significantly (Student's *t* test on paired observations) between rest and activity in those aged 30-50 years (11.82 (SD 1.35) v 12.67 (1.17) kPa, *n*=31, *p*<0.001), 51-70 years (10.79 (1.23) v 11.44 (1.13) kPa, *n*=31, *p*<0.01), and over 70 years (10.20 (1.0) v 11.11 (1.03) kPa, *n*=25, *p*<0.01), but not in the 21 patients aged under 30 (13.13 (0.81) v 1.33 (1.02)). There were no significant differences between the age groups in arterial oxygen saturation.

The moving averages on the observed arterial oxygen tension and saturation values were calculated from patient data ranked by age; these values are shown in the figure plotted in relation to average ages obtained in the same way. As a moving average is a range of mathematical means a standard deviation can be given for every value on the curve. With respect

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