few days later he noticed an area of numbness and paraesthesia below the right rib cage. These symptoms were more pronounced at night. He was otherwise well, though four years previously he had undergone an operation for a left renal stone. He was taking lente insulin 35 units and soluble insulin 10 units each morning, metoprolol for hypertension, and disopyramide and digoxin for a cardiac arrhythmia. He had been admitted to a district general hospital for investigations including ultrasound examination and computed tomography of the abdomen, barium enema, barium meal examination, and intravenous urography. None had shown any abnormality.

On examination he was overweight with a pulse of 60 beats/minute, atrial fibrillation, and blood pressure 160/76 mm Hg without postural hypotension. Fundal examination was normal. There was a definite right sided abdominal swelling (figure) with weakness of the right sided abdominal muscles, though no masses were palpable. Neurological examination showed an area of hyperesthesia with decreased touch in the right T6 and T7 dermatomes anterolaterally. Abdominal reflexes were absent. Sweating was normal in the hands and feet.

Right sided abdominal swelling caused by diabetic truncal polyradiculopathy.

A random blood glucose concentration was 12.3 mmol/l (221 mg/100 ml) and glycosylated haemoglobin 8% (range in non-diabetics 5-7%). Urea and electrolytes, serum B₁₂, and results of liver function tests and urine analysis were normal. A Venereal Disease Research Laboratory test gave a negative result. Nerve conduction studies in the peroneal nerve were normal, though the sural nerve showed evidence of peripheral sensory neuropathy. Electromyography showed fibrillations and positive waves, an increase in the proportion of polyphasic motor unit potentials, and decreased interference patterns in the rectus abdominis innervated by T6-T12 on the right. Similar changes were seen in the right external oblique and thoracic paraspinal muscles. All studies on the left side gave normal results.

Thoracic polyradiculopathy was diagnosed, and the sensory symptoms resolved over two months. No change was seen in the abdominal swelling.

Comment

This patient presented with asymmetrical motor abnormalities in the abdominal muscles and mild and transient sensory symptoms affecting the right T6 and T7 dermatomes. He had electrophysiological evidence of only a mild sensory peripheral neuropathy, and, furthermore, there was no postural hypotension or clinical evidence of decreased sweating in the feet to suggest autonomic neuropathy. We could not perform standard heart rate dependent tests of autonomic function as the patient was in atrial fibrillation. Kikta *et al* reported on one patient with thoracic polyradiculopathy who was found to have abdominal swelling, though the patient was not diabetic and had an eight month history of abdominal pain. The diagnosis was confirmed by electromyography, and although a glucose tolerance test did not confirm diabetes it was suggestive of impaired glucose tolerance,

which may have contributed to the aetiology of the polyradiculopathy.⁵

Truncal polyradiculopathy should be considered in diabetic patients with unexplained abdominal pain or areas of muscle weakness. This case shows that such patients may present with no other neuro-pathic manifestations. If the diagnosis is considered early many unnecessary investigations might be avoided. Electromyography is the most helpful investigation in diagnosing this condition.^{3,5}

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Accumulation of midazolam after repeated dosage in patients receiving mechanical ventilation in an intensive care unit

Midazolam hydrochloride (Hypnovel) is a recently introduced imidazobenzodiazepine. Its potency and rapid onset and short duration of action after a single intravenous bolus make it an ideal agent for premedication or induction in anaesthesia for short surgical, endoscopic, and dental procedures. These same pharmacokinetic features would seem to make the drug an ideal sedative for patients receiving mechanical ventilation. A chance observation of an unusually high plasma midazolam concentration (750 µg/l) in a seriously ill 75 year old needing prolonged intermittent positive pressure ventilation for unexplained respiratory depression, however, led us to examine the problem in three other patients with a similar clinical course.

Present series and results

Samples of serum (after stopping treatment with midazolam) were analysed retrospectively by a sensitive and specific gas-liquid chromatographic method developed at the poisons unit (unpublished data). The terminal half lives were determined by log linear least squares regression analysis.

The figure shows the serial plasma midazolam concentrations in the three patients.

Case 1—A 68 year old man (weight 65 kg) with chronic renal failure, hypertension, and angina developed cardiac failure and pneumonia after a myocardial infarction. Respiratory and cardiac failure necessitated intermittent positive pressure ventilation and inotropic support as well as daily haemofiltration. Sedation was achieved with intravenous midazolam (total daily dosage 5 mg, 40 mg, 40 mg, 70 mg, 45 mg, 5 mg) and papaveretum. He regained full consciousness six days after the last dose of midazolam and eventually recovered.

Case 2—A 46 month old girl (3.6 kg) required intermittent positive pressure ventilation after total correction of her tetralogy of Fallot. She was sedated with intravenous midazolam (total daily dosage 11.5 mg, 32.5 mg, 26.5 mg, 8 mg), papaveretum, and chloral hydrate. She regained consciousness 48 hours after the last dose of midazolam, adequate sedation then being maintained with papaveretum and chloral hydrate at the same dosage. Abnormal coagulation values were ascribed to mild hepatic dysfunction secondary to cardiac failure.

Case 3—A 56 year old man (100 kg) with brittle asthma suffered an acute exacerbation requiring intermittent positive pressure ventilation after failure

of initial treatment. Sedation was achieved with intravenous midazolam (total daily dosage 75 mg, 102.5 mg, 40 mg, 40 mg, 60 mg, 20 mg) while conventional vigorous bronchodilator treatment continued. The day after his last dose of midazolam he was alert enough to be extubated; his further progress was uncomplicated.

Comment

The manufacturer's data sheet recommends that midazolam should be given by single intravenous or intramuscular injection for sedation/induction or premedication respectively. This is based on reported pharmacokinetic studies showing biexponential decay after single intravenous administration, with a terminal half life of about two hours.^{1,2} Caution is advised in elderly patients and when the drug is to be given with other sedatives; midazolam is not advised in children younger than 7 years.

Serial plasma midazolam concentrations after last dose in three patients.

Midazolam is metabolised in the liver to α -hydroxymidazolam, which does not normally contribute to clinical activity as it is rapidly conjugated before being excreted by the kidney.² Thus reduced hepatic clearance secondary to poor liver perfusion or drug interactions with enzyme inhibitors³ may occur, but renal disease should not be important.

In the three patients whose serial plasma midazolam concentrations were measured the terminal half lives were 19.4 hours, 8.9 hours, and 15.8 hours respectively. In each case the period of respiratory depression (and therefore mechanical ventilation) was prolonged and the possibility of a neurological cause considered. This clinically important finding might be explained by reduced hepatic clearance of the drug secondary to pharmacogenetic variation, reduced liver perfusion (as in case 2), or an interaction with an enzyme inhibiting drug (all patients were receiving erythromycin). Alternatively, the elimination half life after chronic dosage may be longer than after a single dose if there is accumulation in tissues with subsequent release (as happens with gentamicin⁴ or if the true elimination half life after a single dose cannot be determined because the plasma drug concentrations are below the detection limit of the assay (as with methaqualone).⁵ In seriously ill patients a combination of these factors may operate.

Our observations do not allow us to distinguish these possibilities in the patients reported but suggest that if midazolam is used in repeated doses accumulation may occur, with a concomitantly prolonged recovery and the need for prolonged mechanical ventilation. Thus until further studies elucidate the mechanism of this phenomenon the recommendations in the manufacturer's data sheet should be followed. This is the first report of prolonged sedation after repeated dosage that the manufacturer has received.

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Alerting close relatives of patients with glaucoma

More than 1% of people aged over 40 in the United Kingdom have chronic open angle glaucoma.¹ It characteristically causes bilateral optic atrophy with progressive reduction of the visual fields and, if untreated, eventually leads to blindness. Over 20 years ago near relatives of people with this form of glaucoma were shown to be at particular risk of developing the disease.² This discovery led to glaucoma family screening clinics being set up in some centres.³ Eye surgeons, however, currently rely on patients themselves to contact their near relatives to suggest that they too should be checked for glaucoma. We examined how effectively this informal system was working at the Southampton Eye Hospital.

Patients, methods, and results

As part of a larger study⁴ 214 patients with glaucoma were interviewed at home by one of us (JMM). All patients were asked, "Do you know what is wrong with your eyes?" Those that knew that they had glaucoma were asked, "Do you realise that glaucoma may run in families?" Finally, those that appreciated the relevance of the family history were asked, "Have you contacted any near relatives to suggest that they too should have their eyes checked?"

Clinicians at this hospital had thought that they explained the consequences of glaucoma to patients, telling them that the disease sometimes runs in families and that they should tell their relatives to have their own eyes checked. Despite this 56 (26.2%) of the patients interviewed did not know that they had glaucoma, though they knew that something was wrong with their eyes, for all of them had attended this hospital many times. All 56 had been prescribed eye drops to be instilled several times a day, sometimes over many years, and some had undergone surgery. Because these patients did not know the name of their eye disease they could not respond to any publicity about glaucoma. In addition, none of these 56 patients knew that they had a disease that might have a hereditary basis.

One hundred and fifty eight patients knew that they suffered from glaucoma. Of them, 70 (44.3%) did not appreciate that this disorder sometimes runs in families despite a booklet on glaucoma, in which the importance of the family history is stressed, being available free in the outpatient department. Many copies of this booklet are taken either by patients or those relatives who bring them to the hospital. Of the 88 patients who realised that they should advise their near relatives to have their eyes checked, only 41 (46.5%) had actually taken steps to contact any such relative, let alone all of them. Thus, of the 214 patients interviewed, only 47 (22%) had alerted a relative that they might have a potentially blinding condition.

Comment

Nowadays, if glaucoma is diagnosed early, patients stand a good chance of retaining at least reasonable vision for the remainder of their lives. In its early stages the disease does not cause symptoms, and many patients do not present until the loss of field is far advanced or complications have set in. The identification of a group at high risk, in the form of near relatives, was a great advance for it pointed the way to identifying economically people with only slight damage to their