

Generalized Seizure Following Subcutaneous Pethidine For Chronic Pain

G Garcea, T Lloyd, D Berry, A Dennison

Citation

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Abstract

A 53-year old female was admitted with chronic pancreatitis requiring pethidine analgesia. Twenty-four hours following admission a brief generalised seizure occurred with incontinence and post-seizure amnesia. Myoclonic jerking preceded the seizure and was also present post-fit. The patient's pain control was changed to diamorphine, with no subsequent adverse effects. On closer questioning the patient had had two previous seizures on previous admissions and in those instances the causal relationship with pethidine had not been identified. This case-report highlights the need for increased awareness regarding pethidine-induced seizures, particularly in clinicians and pharmacists involved in managing conditions associated with chronic pain.

BACKGROUND

Patients with chronic pancreatitis frequently require admission to hospital for control of pain. Pethidine is a common analgesic used in hospitals in the management of abdominal pain, and patients with chronic pancreatitis frequently develop preferences to which analgesia they feel is best suited to the management of their pain. Unlike other opioid analgesics, the active metabolite of pethidine; norpethidine is neurotoxic and may induce fits if sufficient accumulation occurs.

CASE REPORT

A 53 year-old was admitted with severe epigastric pain of 4 days duration. The patient had been diagnosed with chronic pancreatitis 8 years previously secondary to previous alcohol abuse. The patient had been tee-total for the last 5 years. Pethidine, 150mg subcutaneously, every 2 hours was used to control the pain. In twenty-four hours, the patient received 3,600mg of pethidine. The patient was noted to have developed myoclonic jerks of her right arm and leg, thirty minutes before suffering a generalised seizure associated with incontinence and post-seizure amnesia. Myoclonic jerks persisted for a further 24 hours following the seizure, although the frequency was reduced with the use of a benzodiazepine. Serum norpethidine levels were measured and found to be 85% above the upper limit of normal. The patient's analgesia was changed to diamorphine subcutaneously and no further seizures occurred. Closer

questioning revealed two similar incidents on previous admissions, each occurring when the patient had received over 1,500mg of pethidine in a twenty-four hour period. Investigations at that time had not revealed any neurological causes for the seizures.

DISCUSSION

Norpethidine is a neurotoxic metabolite from pethidine. Following intraperitoneal administration of norpethidine in rats, myoclonic jerks, a characteristic splayed posture and episodes of exaggerated shivering were observed at doses of 0.06 to 0.18mmol/kg₁. Seizures were also noted to occur. In human studies, repeated administration of pethidine has been reported to result in central nervous system excitatory effects such as tremors, twitches, multifocal myoclonus and seizures, which directly correlate to levels of norpethidine in plasma₂.

Pethidine-induced seizures have usually been reported after parenteral administration and in instances when cumulative doses of 1,000mg or above have been administered_{3,4,5}. Norpethidine accumulation is more likely to occur in patients with impaired renal function₆, secondary to reduced clearance. Patients normally respond well to supportive measures and the use of a benzodiazepine as a muscle relaxant. Conversion of analgesia to an alternative opioid prevents the seizures from recurring. This case-report highlights the need for increased awareness regarding

pethidine-associated neurotoxicity, particularly in patients with chronic pain who may require repeated doses of pethidine analgesia.

References

1. Plummer JL, Gourlay GK, Cmielewski PL, Odontiaidis J, Harvey I. Behavioural effects of norpethidine, a metabolite of pethidine in rats. *Toxicology* 1995; 95: 37-44.
2. Kaiko RF, Foley KM, Grabinski PY, Heidrich G, Rogers AG, Inturrio CE, Redenberg MM. Central nervous system excitatory effects of meperidine in patients. *Ann Neurol* 1983; 13: 180-185.
3. McHugh GJ. Norpethidine accumulation and generalized seizure during pethidine patient-controlled analgesia. *Anaesth Intensive Care* 1999; 27: 289-291.
4. Mareniella MA. Medical causes of seizure. *Lancet* 1998; 352: 383-390.
5. Kussman BD, Sethna NF. Pethidine-associated seizure in a healthy adolescent receiving pethidine for postoperative pain control. *Paediatr Anaesth* 1998; 8: 349-352.
6. Hochman MS. Meripidine-associated myoclonus and seizures in long-term haemodialysis patients. *Ann Neurol* 1983; 14: 593.

Author Information

Giuseppe Garcea, MD, MRCS

Department of Hepatobiliary Surgery, The Leicester General Hospital

Tom Lloyd, MD, MRCS

Department of Hepatobiliary Surgery, The Leicester General Hospital

David Berry, MD, FRCS

Department of Hepatobiliary Surgery, The Leicester General Hospital

Ashley Dennison, MD, FRCS

Department of Hepatobiliary Surgery, The Leicester General Hospital