

## Seizure induced by a small dose of fentanyl

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### Introduction

Although fentanyl-induced seizures are rarely seen clinically, in animal experiments, high doses of fentanyl induced seizures [1]. The reported clinical cases of seizures were usually associated with a high dose of fentanyl [2]. However, two patients have been reported to have seizures after receiving 100 µg [3] or 200 µg [4] of fentanyl. The following case might be the third report of a patient who had a seizure after the administration of a small dose (100 µg) of fentanyl.

### Case report

A 79-year-old woman (weight, 54 kg) was scheduled for an elective laminoplasty for C3–C7 cervical spondylosis. She had had benign tremors of unknown origin in her upper extremities for 16 years for which she took propranolol (30 mg/day). She had had a cholecystectomy under general anesthesia 6 years previously without any complications. Laboratory data, physical examination, and echocardiography showed no abnormalities. One year previously, a computed tomography (CT) scan of the brain, and an electroencephalogram (EEG) showed normal results (Fig. 1A). She came to the operating room without premedication. Blood pressure was 180/100 mmHg and heart rate was 64 beats·min<sup>-1</sup>. Arterial blood gas analysis showed a pH of 7.475, PaCO<sub>2</sub> of 37.2 mmHg, PaO<sub>2</sub> of 77.9 mmHg, HCO<sub>3</sub><sup>-</sup> of 27.5 mmol·l<sup>-1</sup>, base excess of 4.0 mmol·l<sup>-1</sup>, and AaDO<sub>2</sub> of 22.1 mmHg (FiO<sub>2</sub> = 0.21).

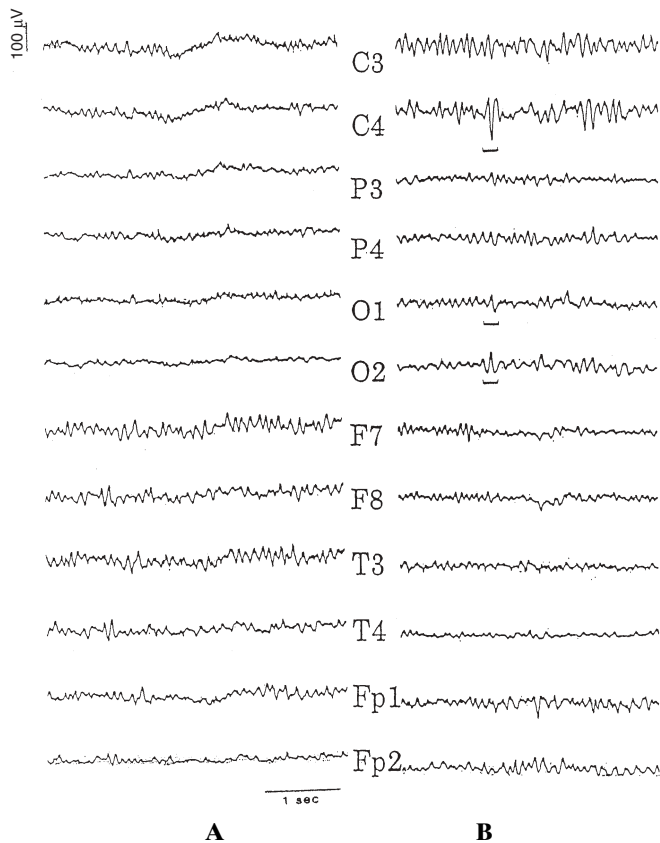
After a venous catheter and a gastric tube were inserted under inhalation of 100% oxygen by mask 50 µg of fentanyl was administered twice 5 min apart, with 1 mg of vecuronium. Approximately 5 min after the second dose of fentanyl, the patient began to show repeated jerking movements of her left hand and arm. Within seconds, similar movements were observed on the right side. She lost consciousness and did not respond to verbal commands. Ventilation by mask was unlabored with no evidence of laryngospasm or muscle rigidity. However, systolic blood pressure increased to over 250 mmHg, diastolic blood pressure to 150 mmHg, and heart rate to 95 beats·min<sup>-1</sup>. Nicardipine (0.5 mg) was administered and systolic blood pressure decreased to below 180 mmHg. After 5 min, the patient regained consciousness spontaneously, but the surgery was postponed.

A CT scan of the brain taken 30 min later showed normal findings. However, magnetic resonance imaging of the brain (MRI) indicated multiple small infarctions in both basal ganglia. Single photon emission computed tomography (SPECT) detected an old defect in the border region between the cerebrum and the cerebellum. A standard 16-lead EEG showed occasional epileptic sharp waves focused on the right central fissure (Fig. 1B).

Phenytoin sodium (200 mg·day<sup>-1</sup>) was administered for 7 days, and the surgery was performed 7 days later. Anesthesia was induced with thiamylal (100 mg) and tracheal intubation was facilitated with vecuronium (7 mg). Anesthesia was maintained with isoflurane (0.8%–1.0%) in oxygen (3 l·min<sup>-1</sup>) and air (2 l·min<sup>-1</sup>). Surgery lasted 3 h and 30 min and no particular problems occurred during or after surgery.

### Discussion

Most patients with seizures have some structural brain lesions or metabolic abnormalities [6]. Idiopathic sei-



**Fig. 1.** **A** Electroencephalogram (EEG) 1 year before surgery. Normal beta waves are seen. **B** EEG immediately after anesthesia. Alpha waves with a few sharp waves focused on the right central fissure were observed

zures occur in children but may persist into adulthood [6]. Cerebrovascular disease is the most common cause of focal or generalized seizures in patients over 50 year of age [7]. Our patient did not have any prior cerebrovascular diseases, although she had tremor of unknown origin. Furthermore, the CT and EEG taken 1 year previously (Fig. 1A) showed no abnormalities. A seizure-like movement developed on the patient's left side during the induction of anesthesia. This was inconsistent with a seizure focus in the left cerebral hemisphere detected by MRI and SPECT after the event. The primary lesion that induces seizure is not always the focus for continuing epilepsy [7].

Carlsson et al. [1] reported seizures with a fentanyl dose of over  $20 \mu\text{g}\cdot\text{kg}^{-1}$  in cats and with higher doses in rats ( $400 \mu\text{g}\cdot\text{kg}^{-1}$ ) and dogs ( $1250 \mu\text{g}\cdot\text{kg}^{-1}$ ). In human, two cases with generalized seizures were reported during rapid intravenous administration of fentanyl ( $44\text{--}78.1 \mu\text{g}\cdot\text{kg}^{-1}$ ) [2]. However, grand mal seizures were reported in two patients who were administered only  $200 \mu\text{g}$  [3] or  $100 \mu\text{g}$  [4] of fentanyl. The present patient also had a seizure when  $100 \mu\text{g}$  of fentanyl was administered.

Partial curarization by 1 mg of vecuronium might be effective, but she did not complain of any abnormal sensation during induction. Scott and Sarnquist [5] suggested two possible mechanisms for seizure induced by fentanyl. One mechanism is that these movements are only exaggerations of fentanyl-induced muscle rigidity that can occur even after a very low dose. The present case might not have resulted from this mechanism because ventilation was unlabored with a mask. The other mechanism is that these abnormal movements are myoclonus secondary to fentanyl-induced depression of inhibitory neurons [5]. Although the seizure in the present case cannot be definitely attributed to fentanyl, only fentanyl was administered before the seizure, and therefore, fentanyl might have induced it.

Even  $100 \mu\text{g}$  of fentanyl might induce seizure in patients with neurological deficits.

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