DELAYED EXCITATORY REACTION FOLLOWING INTERACTION OF COCAINE AND MONOAMINE OXIDASE INHIBITOR (PHENELZINE)

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SUMMARY
A case report is presented in which a patient receiving the monoamine oxidase inhibitor, phenelzine, developed a delayed excitatory reaction following administration of topical cocaine spray during anaesthesia for vocal cord surgery. The pharmacological basis of the drug interaction is discussed.

KEY WORDS

Cocaine was introduced into clinical practice by Koller in 1884. It is a surface anaesthetic of the ester type but, because of systemic effects and the danger of causing dependence, its use is currently confined to topical application in anaesthesia for ear, nose and throat surgery [1]. Monoamine oxidase inhibitors (MAOI) are a group of drugs used in the management of depression, and are known to interact with many drugs used in anaesthetic practice. A case report is presented in which a patient receiving phenelzine medication developed a delayed excitatory reaction following anaesthesia during which topical cocaine spray was administered.

CASE REPORT
A 66-yr-old man weighing 84 kg presented for a Teflon implant to the left vocal cord. He had undergone left pneumonectomy for carcinoma of the bronchus 3 years earlier, at which time the left recurrent laryngeal nerve had been damaged. He had also undergone two subsequent implant procedures under general anaesthesia without adverse effects. Ten years previously, he had an inguinal hernia repair under general anaesthesia, which had been uneventful. Since the last Teflon implant, he had started medication with phenelzine 15 mg twice daily for depression. He had been taking phenelzine up to the time of surgery.

At the preoperative visit, the patient gave no family history of malignant hyperpyrexia and had no known allergies. Clinical examination revealed no abnormalities, resting arterial pressure was 130/85 mm Hg and heart rate 75 beat min⁻¹. Routine tests showed a plasma potassium concentration of 4.6 mmol litre⁻¹. No premedication was ordered, but the morning dose of phenelzine was administered.

Anaesthesia was induced with thiopentone 500 mg, and muscle paralysis produced with suxamethonium 100 mg and gallamine 8 mg. The vocal cords were sprayed with 1 ml of 10% cocaine spray (as on the two previous implant procedures), and the trachea was intubated with a 5.0-mm microlaryngeal tube. Diazemuls 10 mg was given and anaesthesia maintained with nitrous oxide and 0.5% isoflurane in oxygen. No pethidine or other opioid was administered. The procedure lasted 10 min, during which time arterial pressure remained unchanged and the heart rate regular, with no tachycardia. There was no clinical evidence of muscular rigidity or pyrexia.

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Thirty minutes after completion of the surgery, the patient had regained consciousness and was returned to the ward. He was responding appropriately to commands; heart rate was regular at 80 beat min⁻¹, arterial pressure 130/80 mm Hg and ventilatory frequency 16 b.p.m. Thirty minutes after his return to the ward, the patient was discovered by the staff to be unconscious, with generalized coarse tremors and marked muscle rigidity. The heart rate was regular (110 beat min⁻¹) and the arterial pressure 110/60 mm Hg. Rectal temperature was 41.5 °C. He was returned immediately to the recovery room, given 40% oxygen via a Ventimask and cooled using wet blankets and i.v. fluids. Arterial blood-gas analysis showed pH 7.37 (hydrogen ion concentration 42.7), \(P_{\text{aCO}_2}\) 5.5 kPa, \(P_{\text{aO}_2}\) 19.8 kPa, standard bicarbonate 23.5 mmol litre⁻¹ and base excess -1 mmol litre⁻¹. Blood biochemistry showed sodium 136 mmol litre⁻¹, potassium 5.1 mmol litre⁻¹ and urea 6.5 mmol litre⁻¹.

During the following 30 min the patient's tremor resolved and the temperature decreased to 39.0 °C. Within 7 h he had become fully conscious and orientated, and the core temperature had decreased further to 37.0 °C. Over the next 6 days he remained well, but complained of weakness and generalized muscular pains.

**DISCUSSION**

Cocaine potentiates the effects of the catecholamines and the possibility of an adverse drug reaction occurring when cocaine and MAO I are combined is well recognized [2].

Our patient was thought initially to have developed malignant hyperpyrexia, and steps were taken to treat him accordingly. This diagnosis was excluded subsequently as the patient had no family history of the condition, and had previously undergone two similar procedures under general anaesthesia without incident. Blood-gas analysis and serum biochemistry measurements showed no evidence of metabolic acidosis or hypercapnia, and serum potassium concentrations were 5.1 mmol litre⁻¹, compared with a preoperative value of 4.6 mmol litre⁻¹.

Cocaine toxicity was considered. Cocaine blocks the re-uptake of noradrenaline and exogenous catecholamines and the symptoms and signs are those of sympathetic overactivity. These may be manifest as excitement, anxiety, headache, tachycardia and hypertension, while more severe effects include convulsions and coma. The toxic dose quoted for cocaine in adults ranges from 1.0–1.5 mg kg⁻¹ [1] to 3 mg kg⁻¹ [3, 4]. The patient weighed 84 kg and received a dose of 100 mg. He had received the same dose on two previous occasions without toxic effects. Cocaine is absorbed rapidly from the trachea, with peak concentrations occurring at 5 min [5], and our patient showed no evidence of toxicity during operation or for 30 min thereafter. It is possible that the delay in the onset of the symptoms was because of the use of thiopentone and diazepam which would both exert a cerebral depressant action, and might mask the clinical features of toxicity in the initial stages. However, the patient recovered full consciousness before being returned to the ward and at this time showed no evidence of sympathetic overactivity.

The MAOI drugs inhibit the enzyme involved in the metabolic breakdown of catecholamines and increase concentrations of amine neurotransmitters. The combination of cocaine and phenelzine could interact to result in a clinical picture of sympathetic stimulation. This synergism would be expected to manifest soon after the administration of the two drugs, but the patient showed no evidence of sympathetic overactivity during operation or for 30 min after operation. In addition, the symptoms of the patient's reaction are not typical of sympathetic overactivity and the time course of their occurrence would exclude this diagnosis.

The interaction of the MAOI with many anaesthetic agents, especially those with the opioids, is well recognized. Stack, Rogers and Linter have reviewed the subject and described two forms of interaction—excitatory and depressive [6]. The excitatory form is characterized by agitation, headache, hyper- or hypotension, muscular rigidity, hyperpyrexia, convulsions and coma. Based on studies in animals, the excitatory reaction typically seen with MAOI and pethidine is thought to be caused by a block of neuronal uptake of cerebral 5-hydroxy tryptamine (5HT) [7, 8], and work in mice linking increasing toxicity of pethidine with increasing concentrations of cerebral 5HT would support this [9]. In a series of animal experiments cocaine was used to augment amine responses to 5HT, and it was noted that cocaine considerably reduced the inactivation of 5HT [10]. It has been suggested also that a critical concentration of 5HT is required to trigger the excitatory form of the reaction [11].
It is possible that our patient experienced an excitatory reaction because of the increased concentrations of 5HT following interaction of cocaine and phenelzine. A critical concentration of 5HT is required to trigger the reaction, which would account for the delay in the onset of the patient's symptoms.

REFERENCES


