Case Report

Suxamethonium-induced hyperkalaemia 6 weeks after chemoradiotherapy in a patient with rectal carcinoma

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Suxamethonium causes an efflux of potassium (K\(^{+}\)) ions by depolarizing acetylcholine receptors within the neuromuscular junction and produces a transient, small rise in serum K\(^{+}\) concentration in normal individuals that is usually of little clinical importance. Despite the clear efficacy and relative safety of suxamethonium in many patients, anaesthetists are also very aware that acute, severe hyperkalaemia resulting in important cardiovascular sequelae (e.g. malignant ventricular arrhythmias, cardiac arrest) may also occur with administration of suxamethonium in susceptible patients, including those with skeletal muscle injury or thermal trauma. In the current report, we describe a patient with rectal cancer initially treated with chemoradiotherapy who developed hyperkalaemia after suxamethonium and further discuss the potential factors that contributed to this response.

Keywords: complications, hyperkalaemia; complications, skeletal muscle injury; drug, capecitabine; neuromuscular block, suxamethonium; radiation therapy

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Suxamethonium has been a very useful drug in anaesthetic practice since its clinical introduction over 50 yr ago because it produces intense, ultra-short-acting neuromuscular block within 1 min of i.v. injection, thereby facilitating rapid endotracheal intubation. Suxamethonium causes an efflux of potassium (K\(^{+}\)) ions by depolarizing acetylcholine receptors within the neuromuscular junction and produces a transient, small rise in serum K\(^{+}\) concentration in normal individuals that is usually of little clinical importance. Despite the clear efficacy and relative safety of suxamethonium in many patients, anaesthetists are also very aware that acute, severe hyperkalaemia resulting in important cardiovascular sequelae (e.g. malignant ventricular arrhythmias, cardiac arrest) may also occur with administration of suxamethonium in susceptible patients, including those with skeletal muscle injury or thermal trauma. In the current report, we describe a patient with rectal cancer initially treated with chemoradiotherapy who developed hyperkalaemia after suxamethonium and further discuss the potential factors that contributed to this response.

Case report

A 61-yr-old, 185 cm, 109 kg man with a history of stage T3N0 rectal adenocarcinoma was scheduled to undergo a low anterior resection of the distal sigmoid colon and rectum with sphincter preservation during general anaesthesia. The patient had received preoperative lower abdominal and pelvic irradiation (total radiation dose of 50.4 Gy in divided fractions over 6 weeks; 1 Gy=100 rad) and adjuvant chemotherapy [capecitabine 1800 mg per os twice a day before and after each radiation treatment; capecitabine is an orally administered fluoropyrimidine with a pharmacological mechanism of action that is similar to 5-fluorouracil (5-FU)] and had completed this chemoradiation regimen 6 weeks before presenting to the operating room. The patient tolerated the chemoradiotherapy well with the exception of a single episode of radiation-induced enteritis that occurred several weeks before surgery and required brief hospitalization for treatment of dehydration with i.v. fluids. Mucositis was not observed during or after capecitabine treatment nor did
renal toxicity occur. The patient had a past medical history of obesity, chronic low back pain treated with amitriptyline, essential hypertension for which he received lisinopril, and type II diabetes mellitus treated with glyburide and metformin. All medications were withheld on the evening before surgery. Previous general anaesthetics for fusion of the thoracolumbar spine and repair of a right lower extremity fracture were unremarkable.

The patient was premedicated with i.v. midazolam (3 mg) and fentanyl (1 μg kg\(^{-1}\)). A right radial arterial catheter was inserted using local anaesthesia. A preoperative arterial blood gas tension analysis obtained with the patient breathing room air was normal (\(\text{pH} = 7.38\), \(P_{\text{aO}_2} = 90\) mm Hg, \(P_{\text{aCO}_2} = 38\) mm Hg). The preoperative serum potassium (\(K^+\)) and blood glucose concentrations were 4.5 mEq litre\(^{-1}\) and 197 mg dL\(^{-1}\), respectively. Renal function and other serum electrolytes were normal. Induction of anaesthesia was performed using i.v. propofol (2 mg kg\(^{-1}\)), fentanyl (2 μg kg\(^{-1}\)), and suxamethonium (1.5 mg kg\(^{-1}\)). After endotracheal intubation, anaesthesia was maintained with sevoflurane (end-tidal concentrations of 0.7–1.2 minimum alveolar concentration), fentanyl (1–2 μg kg\(^{-1}\) h\(^{-1}\)), and vecuronium (intermittent bolus doses of 0.03 mg kg\(^{-1}\) guided by neuromuscular monitoring). Arterial blood gas tension and serum electrolyte concentration analyses obtained after the abdominal incision revealed the presence of hyperkalaemia (\(K^+ = 6.4\) mEq litre\(^{-1}\)) without evidence of respiratory or metabolic acidosis. Blood glucose concentration was unchanged. A second laboratory study confirmed these findings. No arrhythmias were temporally observed nor were large increases in T-wave amplitude present in leads II or V\(_5\) of the electrocardiogram.

Hyperkalaemia was treated with hyperventilation, sodium bicarbonate (100 mEq), and the combination of 50% dextrose (100 ml) and s.c. insulin (10 units). Ten minutes after these initial interventions, \(K^+\) was reduced to 5.6 mEq litre\(^{-1}\), and subsequent administration of additional s.c. insulin (5 units) further decreased \(K^+\) to 4.4 mEq litre\(^{-1}\). The remainder of the surgical procedure was uneventful. The patient made an unremarkable recovery and was discharged from the hospital on the 14th postoperative day.

**Discussion**

Ionizing radiation causes less pronounced damage to skeletal muscle when compared with other tissues. Nevertheless, skeletal muscle exposed to radiation (doses between 5 and 60 Gy) may display microvascular damage,\(^5\) oedema,\(^6\) and chronic degenerative injury\(^7\),\(^8\) in a time- and dose-related manner independent of acute necrosis.\(^7\),\(^9\),\(^10\) These radiation-induced alterations in skeletal muscle were proposed to be morphologically similar to those observed in Duchenne’s muscular dystrophy,\(^11\) a known risk factor for suxamethonium-induced hyperkalaemia.\(^1\) Although such a comparison may not be entirely accurate from a pathophysiological perspective, it is clear that radiation therapy produces a form of chronic thermal injury in skeletal muscle that may precipitate hyperkalaemia in response to administration of depolarizing neuromuscular blockers.\(^1\) To our knowledge, only a single previous investigation examined the effects of radiation injury on suxamethonium-induced hyperkalaemia *in vivo*.\(^12\) Cairoli and colleagues\(^12\) conducted their experimental investigation in rats after a case of suxamethonium-induced hyperkalaemic cardiac arrest occurred in an otherwise healthy patient undergoing radiation therapy for treatment of a lower extremity sarcoma. The authors\(^12\) demonstrated that suxamethonium (3 mg kg\(^{-1}\)) produced hyperkalaemia (peak \(K^+ = 7.7\) (0.5) mEq litre\(^{-1}\) 5 min after administration; data are mean (SEM)) in rats 3 weeks after total body exposure to fractionated irradiation (total dose of 25 Gy) but not after 1 week. These results indicated for the first time that remote radiation exposure to skeletal muscle may precipitate hyperkalaemia in response to administration of depolarizing neuromuscular blockers. The findings further suggested that the upregulation of acetylcholine receptors implicated in the pathogenesis of suxamethonium-induced hyperkalaemia during other forms of skeletal muscle damage (e.g. burns, crush injury, and prolonged immobilization) may also occur after radiation therapy.\(^1\),\(^4\),\(^12\)

The time course, relative severity, and dose-dependency of sensitivity to depolarizing neuromuscular blockers after radiation therapy have yet to be comprehensively evaluated. However, the current case suggests that a 6 week interval after the completion of a fractionated course delivering approximately 50 Gy of irradiation to the lower abdomen and pelvis for the treatment of rectal carcinoma was adequate to cause moderate hyperkalaemia (defined as a serum \(K^+\) concentration between 6.1 and 6.9 mEq litre\(^{-1}\)) in response to administration of the usual intubating dose of suxamethonium in our patient. Fortunately, our patient did not develop any major cardiac sequelae before the diagnosis of hyperkalaemia was established. The use of chemotherapeutic agents (such as capecitabine or 5-FU) that enhance the efficacy of radiation therapy has been shown to improve local control, distant control, and overall survival in patients with locally advanced, non-metastatic rectal cancer.\(^14\),\(^15\) Whether this chemoradiotherapy approach produces more pronounced skeletal muscle injury and thereby further increases subsequent susceptibility to suxamethonium-induced hyperkalaemia is unknown. However, our patient maintained body weight during the preoperative chemoradiotherapy and did not display evidence suggesting profound physical deconditioning or frank skeletal muscle degeneration that may have suggested an increased risk for hyperkalaemia after administration of suxamethonium. Hyperkalaemia of suxamethonium has also been previously reported in patients with chemotherapy-induced mucositis,\(^16\) but our patient did not develop any evidence of this side-effect during or after the 6-week course of chemoradiotherapy.
Our patient had no other known risk factors for suxamethonium-induced hyperkalaemia, as described in a recent comprehensive review. Suxamethonium has been shown to increase serum K\(^+\) concentration by 0.5–1.0 mEq litre\(^{-1}\) in normal individuals, and this modest response usually resolves within 15 min after administration of the drug.\(^2\)\(^3\) The use of suxamethonium has also been shown to be safe (as indicated by an absence of arrhythmias or other morbidity) in patients with preoperative serum K\(^+\) concentrations of 5.6 mEq litre\(^{-1}\) or greater.\(^1\) Thus, it seems highly unlikely that our patient had an exaggerated increase in K\(^+\) concentration (1.9 mEq litre\(^{-1}\)) in response to administration of suxamethonium, and a prolonged duration of this hyperkalaemia could be solely attributed to normal variation. Nevertheless, such an individual variability cannot be entirely excluded and remains a possible (although remote) explanation for the observed clinical course. The authors used a dose of suxamethonium (1.5 mg kg\(^{-1}\)) to facilitate endotracheal intubation which exceeded the dose that had been recently recommended (1.0 mg kg\(^{-1}\)).\(^1\)\(^8\)\(^9\) and it is possible that this larger dose may have contributed to the pronounced hyperkalaemic response observed in our patient. However, Powell and Miller\(^2\) demonstrated that repetitive 1.0 mg kg\(^{-1}\) doses of suxamethonium (1.5 mg kg\(^{-1}\)) to facilitate endotracheal intubation did not produce increases in serum K\(^+\) concentrations greater than 0.6 mEq litre\(^{-1}\) in healthy patients or those with renal failure. Thus, it also appears unlikely that the hyperkalaemia observed in our patient was related to a dose-dependent effect. On the basis of the current case and previous data,\(^1\)\(^2\) the precise incidence, severity, duration, and clinical consequences of suxamethonium-induced hyperkalaemia in cancer patients after chemoradiotherapy deserves to be more thoroughly investigated.

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