





Anesthetic Care During Tracheostomy in a Patient with Generalized Tetanus: A Case Report

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Abstract: Tetanus is a potentially fatal infectious disease caused by the toxins produced by the anaerobic bacterium, *Clostridium tetani*. Of major concern during the perioperative care of these patients is control of muscle spasms, skeletal rigidity, and autonomic dysfunction. Several of the modern sedative and opioid agents including remifentanyl have not been fully evaluated in managing tetanus. We present the intraoperative use of remifentanyl in a 75-year-old woman with generalized tetanus who required anesthetic care during placement of a tracheostomy. The end-organ involvement of tetanus is presented, previous reports of anesthetic care reviewed, and the potential utility of remifentanyl explored.

Keywords: tetanus, tracheostomy, general anesthesia

Introduction

Tetanus is a fatal infectious disease caused by the toxins, tetanospasmin and tetanolysin, produced by the anaerobic bacterium, *Clostridium tetani*.¹ Generalized tetanus with skeletal muscle rigidity, muscle spasms, and autonomic nerve dysfunction frequently requires endotracheal intubation and mechanical ventilation with deep sedation and neuromuscular blockade. Mechanical ventilation may be required in up to 77.5% of the patients with tetanus with a median duration of ventilation of 23 days, and 80% of the patients requiring tracheostomy. Although the mortality of severe tetanus is as high as 37–50% in low-income and middle-income countries, the in-hospital mortality has been reported to be 6.8% in Japan.^{1,2}

The ICU and anesthetic care of patients with generalized tetanus may be complicated by difficulties with control of the autonomic dysfunction and skeletal muscle rigidity. Several of the modern sedative and opioid agents including remifentanyl have not been fully evaluated in managing tetanus. We present the intraoperative use of remifentanyl in a 75-year-old woman with generalized tetanus who required anesthetic care during placement of a tracheostomy. The end-organ involvement of tetanus is presented, previous reports of anesthetic care reviewed, and the potential utility of remifentanyl explored. Presentation of this case report is in line with the guidelines of the Institutional Review Board of Yokohama Municipal Citizen's Hospital (Yokohama, Japan). Written Informed consent for publication was obtained from the patient.

Case Presentation

The patient was a 75-year-old, 72-kg woman who presented for surgical tracheostomy for the management of generalized tetanus. Her past medical history was significant for

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bronchial asthma and hypertension. Her medication regimen included nifedipine 10 mg once a day, trichlormethiazide 1 mg once a day, pranlukast hydrate 112.5 mg twice a day, theophylline 400 mg twice a day, cloperastine hydrochloride 40 mg twice a day, and dimethicone 240 mg three times a day. Five days prior to hospital admission, she suffered a laceration to her right heel. As she had not been recently vaccinated against tetanus, 1500 units of human tetanus immunoglobulin were administered. However, signs and symptoms progressed and she was admitted to the intensive care unit (ICU) because of severe trismus, generalized spasticity, dysphagia, and violent autonomic disturbances involving the cardiovascular system. Her trachea was intubated, mechanical ventilation initiated, and plans made for a surgical tracheostomy on the second day. Her medication regimen in the ICU included fentanyl (35 µg/hr), propofol (2 mg/kg/hr), dexmedetomidine (0.2 µg/kg/hr), midazolam (0.05 mg/kg/hr), landiolol (1 µg/kg/min), and magnesium sulfate of (0.5 g/hr). The serum magnesium level was 6.9 mg/dL on the day of surgery. Despite the continuous infusion of these sedative and analgesic agents as well as the supra-therapeutic magnesium level, she had episodes of sudden autonomic dysfunction with a rapid increase in her systolic blood pressure to ≥ 200 mmHg several times per day. A transthoracic echocardiography revealed normal ventricular contractility. Tracheostomy was performed on the seventh day. She was transported to the operating room, and routine American Society of Anesthesiologists' monitors were placed. A bolus of propofol (30 mg) and rocuronium (30 mg) were administered prior to the transfer to the operating room table. General anesthesia was maintained with total intravenous anesthesia (TIVA) using a continuous infusion of propofol (3 mg/kg/hr), remifentanyl (0.1–0.25 µg/kg/min), and rocuronium (0.8 mg/kg/hr). Landiolol and the magnesium sulfate infusion were continued during the procedure. The systolic blood pressure ranged from 90 to 120 mmHg with a heart rate of 45–55 beats/minute. The surgical procedure required approximately 30 minutes. Remifentanyl was discontinued at the end of the surgery. Postoperative sedative and analgesia agents included 2 mg/kg/hr of propofol, 35 µg/hr of fentanyl, 0.2 µg/kg/hr of dexmedetomidine, and 0.1 mg/kg/hr of midazolam. Despite continuing these sedative and analgesic infusions, hypertension and tachycardia were intermittently observed after the patient was transported back to the ICU. However, these hemodynamic changes did not require further pharmacologic treatment. The continuous infusion of midazolam was discontinued on the 32nd hospital day. The continuous infusions of propofol and fentanyl were discontinued on the 37th hospital day. After that time, the patient was transitioned

from mechanical ventilation to spontaneous ventilation, and subsequently transferred to the general inpatient ward from the ICU on the 41st hospital day. Although she needed a continuous rehabilitation program to recover motor function, she recovered without neurological deficit. She was discharged from the hospital and transferred to the rehabilitation hospital on the 69th day of hospitalization.

Discussion

The clinical features of tetanus are caused by tetanospasmin (a metalloprotease). It enters the peripheral nervous system directly from the contaminated wound, affecting the function and transmission of motor, sensory, and autonomic neurons. Tetanospasmin travels through axons in a retrograde fashion to the central nervous system (CNS). Radiolabelled assays have demonstrated that tetanospasmin has a preference for inhibitory motor neurons, which explains the clinical picture of muscle rigidity. The tetanus toxin disturbs formation of the soluble N-ethylmaleimide-sensitive factor attachment protein receptor (SNARE) complex, which decreases motor nerve inhibition, resulting in the characteristic muscle spasm.³ Tetanus toxin also has activity at the central excitatory synapses, binding to sympathetic adrenergic neurons, leading to autonomic dysregulation and episodes of hypertension.⁴

During anesthetic care of patients with severe tetanus, control of skeletal muscular rigidity, muscle spasms, and autonomic dysfunction may be problematic.^{5,6} As the majority of reports of anesthetic care for such patients are anecdotal, there is limited evidence-based medicine to guide clinical practice. Additionally, as many of these reports are from developing countries, there is limited experience with novel sedative and opioid agents such as remifentanyl. To date, the benzodiazepines remain the primary agents that have been used most commonly to control muscle spasms and rigidity related to tetanus.^{1,7} Neuromuscular blocking agents may be added when sedatives are ineffective enough. Recently, anecdotal information from single-case reports or case series have demonstrated the potential utility of dexmedetomidine (0.2–0.7 µg/kg/hr) to control muscle spasms and autonomic dysfunction.^{8,9}

Remifentanyl is a selective mu-opioid receptor agonist, which has a rapid onset of action and is metabolized by non-specific ester hydrolysis in the blood and tissues.¹⁰ During surgical procedures, noxious stimuli and surgical incision may precipitate muscle spasms and autonomic dysfunction. Potent opioids such as fentanyl and its derivatives are frequently used to blunt the surgical stress

response and the response to noxious surgical stimuli. In our patient, remifentanyl was discontinued in the OR because continuous infusion of remifentanyl is forbidden in Japan. Although other sedative agents were administered in the ICU, her cardiovascular status was more stable during the remifentanyl infusion in the OR than in the ICU.

In our patient, autonomic dysfunction and muscle rigidity persisted despite the administration of propofol, dexmedetomidine, and midazolam during her initial time in the ICU. Therefore, a magnesium sulphate infusion was added with limited efficacy in an attempt to control these clinical manifestations of tetanus.^{11,12} Despite its limited efficacy in our patient, magnesium sulphate was routinely used to control muscle rigidity and autonomic dysfunction with tetanus as it may reduce the requirement for other medications in this clinical setting.^{12,13} Although not noted in our patient, potential concerns regarding the administration of magnesium include skeletal muscle weakness, sedation, hypotension, and bradyarrhythmias.¹³

Given the persistence of clinical symptoms of tetanus despite the administration of midazolam, fentanyl, propofol, dexmedetomidine, magnesium, and landiolol; a remifentanyl infusion was added to control the surgical stress response during tracheostomy. Although we noted no hemodynamic effects of the remifentanyl infusion, its short-life allows for rapid dissipation of its clinical effects if hemodynamic depression is noted. Additionally, as a potent μ -agonist, it effectively controls the response to surgical manipulation.

To date, we could find only one previous report regarding the use of remifentanyl in a patient with tetanus. Beecroft et al reported the use of a remifentanyl to control the systemic manifestations of severe generalized tetanic spasms in a 61-year-old woman which were refractory to infusions of propofol, midazolam, alfentanil, magnesium sulphate, and atracurium.¹⁰ The muscle spasms were severe enough to result in chest wall rigidity, which compromised mechanical ventilation even with manual bag-valve ventilation, occurring in response to even minor stimuli. A remifentanyl infusion was started at 0.05–0.1 $\mu\text{g}/\text{kg}/\text{min}$. The infusion rate was increased prior to any therapies and titrated to effect (0.3–0.6 $\mu\text{g}/\text{kg}/\text{min}$). This controlled the muscle spasms sufficiently to allow therapy to continue without the need for neuromuscular blockade and a reduction of the propofol infusion to 0.5–2 $\text{mg}/\text{kg}/\text{hr}$. The propofol and remifentanyl infusions were continued for a total of 2 weeks. After cessation of sedation, there were concerns regarding the patient's neurologic status and

a potential hypoxic brain injury. The patient subsequently developed severe bronchopneumonia, and in view of the associated concerns regarding brain injury, treatment was not escalated and the patient expired on day 18.¹⁰

In summary, our case and the report of Beecroft et al demonstrate anecdotal experience regarding the potential efficacy of remifentanyl in controlling the autonomic dysfunction and muscle spasms associated with tetanus. Given its potent effects as a μ -agonist, it provides intense analgesia to both noxious and surgical stimuli. Its short half-life allows for rapid titration by continuous infusion, thereby making in a potentially useful adjunct to other agents commonly used to control the clinical manifestations of tetanus.

Abbreviations

ICU, intensive care unit; TIVA, total intravenous anesthesia; CNS, central nervous system; SNARE, soluble N-ethylmaleimide-sensitive factor attachment protein receptor.

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Disclosure

The authors do not have conflicts of interest.

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