

# IMPOSSIBLE MASK VENTILATION AFTER AN UNUSUALLY LOW DOSE FENTANYL-INDUCED MUSCLE RIGIDITY IN A PATIENT WITH ESSENTIAL TREMOR: A CASE REPORT AND REVIEW OF THE LITERATURE

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## Abstract

Although opioid-induced muscle rigidity occurs more commonly with large doses and rapid administration of the drugs, there is a number of cases reported, where muscle rigidity was experienced with lower doses of opioids. We present and discuss a case of muscle rigidity induced by an unusually low dose of fentanyl as primary agent during induction of anesthesia. A 79 year old male patient, scheduled for hernia repair, and with a preoperative physical examination of slight hand tremor, received a bolus of 100mcg (1.2mcg/kg) fentanyl as primary agent for induction. About 40sec later he stopped responding, lost consciousness and developed neck and masseter muscle spasm with jaw closure and thoracoabdominal rigidity. Blood pressure was increased significantly. Ventilation was impossible. Rapid oxygen desaturation led us to proceed with IV propofol 150mg and suxamethonium 100mg. Opioid-induced muscle rigidity may cause life-threatening respiratory compromise and should be readily recognized and treated by anesthesiologists.

**Key words:** Anesthesia, opioids, muscle rigidity, essential tremor.

## Introduction

Opioid administration produces intense analgesia and decreased sympathetic response to attenuate stress response to painful surgical stimulation. Because of these advantageous clinical properties, opioids have increasingly seen wide-spread use in anesthesia. Unfortunately, the profound analgesia of high-dose opioid administration may be accompanied by prolonged respiratory depression and intense muscle rigidity. Opioid-induced muscle rigidity was first described by Hamilton and Cullen in 1953<sup>1</sup>. At the same time with the introduction of fentanyl in anesthetic practice (1981), fentanyl-induced muscle rigidity started to be reported both in adults and children<sup>2,3,4</sup>. Thereafter, muscle rigidity after opioid administration became a well documented effect, most commonly with lipophilic synthetic opioids such as fentanyl, alfentanil, remifentanil and sufentanil, although its pathophysiology is not as well clarified<sup>5-7</sup>. It is not a common adverse effect and its true incidence is unknown.

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The development of muscle rigidity accompanies induction of anesthesia with opioids and in most cases has been reported in preterm and term infants or after administration of high doses of opioids<sup>8-12</sup>. However, a recent case report<sup>13</sup> concerning fentanyl-induced muscle rigidity during sedation for bronchoscopy, increased the concern about the safety of opioid administration in minor interventions requiring sedation that is very common in the everyday anesthetic practice. There are other cases where muscle rigidity has been induced after low doses of opioids but in accordance with other factors<sup>14-15</sup>. The usual clinical presentation varies from mild symptoms of muscle spasm, up to severe and potentially life-threatening symptoms like inability of ventilation and clonus. We report a case of muscle rigidity induced by an unusually low dose of fentanyl as primary agent during induction of anesthesia.

### Case History

A 79 year old male patient (height 177cm, weight 82kg) with history of arterial hypertension and coronary artery disease under treatment, was scheduled for hernia repair. Preoperative physical examination performed revealed slight hand tremor and otherwise was normal. His laboratory results were normal. The patient did not receive premedication. In the operating room standard monitoring was applied and the patient was preoxygenated and received a bolus of 100µg fentanyl as primary agent for induction, in order to attenuate the response to laryngoscopy. About 40sec later he stopped responding, lost consciousness and developed neck and masseter muscle spasm with jaw closure, thoracoabdominal rigidity, upper limb flexion and lower limb extension without any sign of lateralization. Blood pressure increased significantly (from 125/80mmHg to 195/110mmHg). Ventilation was impossible even with four-handed bag-mask ventilation. The inability to open the mouth due to masseter muscle spasm made it impossible to insert an oropharyngeal or laryngeal mask airway. A nasopharyngeal airway was inserted and mask ventilation was initiated with no improvement. Rapid oxygen desaturation (SpO<sub>2</sub> <85%) led us to proceed with IV propofol (150mg) and suxamethonium (100mg). Subsequently, the muscle spasm subsided and

ventilation and oxygenation were resumed successfully with an increase of SpO<sub>2</sub> to 100%. Laryngoscopy and tracheal intubation were successful. The operation was completed uneventfully and the patient awakened one hour later. When questioned postoperatively the patient had no recall of the event. After neurology consultation the patient was submitted to a CT and MRI scan which were normal. The postoperative complete neurology examination concluded that the patient suffered from essential tremor.

### Discussion

We reported a case of an unusually low dose fentanyl-induced muscle rigidity. Since the patient did not receive any premedication and fentanyl was the sole agent during induction, there is no doubt for the cause of muscle rigidity. To our knowledge this is the first case of muscle rigidity with such a low dose of fentanyl (1.2mcg/kg) and so early (40sec) at induction. Low dose opioid-induced rigidity have been reported in preterm and term infants, or patients with risk factors like neurological diseases, metabolic disorders and medications modifying dopamine levels<sup>8,10,14,15</sup>. Our patient was only receiving antihypertensive therapy including an ACE inhibitor and a beta adrenoreceptor antagonist. The essential tremor which was diagnosed postoperatively could have been a contributing role.

When used intraoperatively, the administration of a nondepolarizing neuromuscular blocking agent concurrently with fentanyl prevents rigidity<sup>16,17</sup>. Although chest wall rigidity occurs more commonly with large doses and rapid administration, there is a number of cases reported, where muscle rigidity was experienced with lower doses of opioids<sup>13,14</sup>. Although most common with the rapid administration of large doses, this rare adverse effect may occur with small doses especially in neonates and infants<sup>8-11,14</sup>. Additionally, this occurred in our case as well as in a patient undergoing bronchoscopy<sup>13</sup>. Skeletal muscle rigidity has been recognized, most commonly with lipophilic synthetic opioids such as fentanyl, alfentanil, remifentanyl, and sufentanyl. This rigidity can primarily affect the chest and abdominal musculature, resulting in the “wooden chest syndrome.” Chest wall rigidity

decreases chest wall compliance and may result in ineffective spontaneous ventilation and may also make assisted ventilation more difficult<sup>5,18</sup>.

The ventilatory difficulty may be contributed to vocal cords closure, to the jaw closure and the thoraco-abdominal rigidity<sup>20,21</sup>. Although a nasopharyngeal airway can be inserted, airway obstruction caused primarily by glottis closure, may make it difficult to ventilate the patient manually. The incidence of glottis closure in patients with opioid induced muscle rigidity ranges from 50-100% depending on the opioid used, the dose and the rate at which it is administered<sup>21</sup>. Although Muller and Vogtmann<sup>22</sup> reported the adverse effects to be self-limited and brief, all other case reports required treatment with naloxone administration, neuromuscular blockade, and/or mechanical ventilation. Pretreatment with an alpha-2 adrenergic agonist (clonidine and dexmedetomidine) has been shown to decrease the incidence of opioid-induced rigidity, whereas serotonergic agents have been found effective in animal studies<sup>23,24</sup>.

In our case the patient lost consciousness simultaneously with opioid-induced rigidity. This is in accordance with Streisand et al<sup>25</sup> in a study in human volunteers. They reported that all subjects lost consciousness simultaneously with opioid-induced rigidity. Fentanyl was administered at a rate of 150 mcg/min and rigidity occurred at a dose of 15 mcg/kg<sup>25</sup>. The onset of rigidity and unconsciousness occurred an average of 3 min after peak fentanyl plasma concentrations and was associated with plasma fentanyl concentrations consistent with drug action<sup>25</sup>. In contrast Grell et al<sup>26</sup> reported that, 11 of 12 patients developed rigidity that neither produced unconsciousness nor impaired spontaneous ventilation. Waller et al<sup>27</sup> reported that patients could open their eyes to command and initiate a breath, despite the presence of chest wall rigidity during induction in anesthesia with fentanyl. However, in the studies of both Grell et al and Waller et al, fentanyl was administered at slower rates (30 and 50 mcg/min respectively) and chest wall rigidity occurred at doses of 7.3 and 8 mcg/kg respectively. It appears that a mild form of rigidity, associated with decreased chest wall compliance, can be detected with maintenance of consciousness and spontaneous ventilation. In our

case fentanyl 100 mcg was given on a bolus which is common practice during induction in anesthesia. Rigidity occurred very early after 40sec, and at an unusually low dose of 1.2mcg/kg. Additionally, our patient became hypertensive with muscle rigidity. This is in accordance with other studies, since muscle rigidity does not affect only the respiratory system, but additionally induces significant hemodynamic changes, accompanied by CO<sub>2</sub> retention<sup>3,13</sup>.

The exact mechanism of increased muscle tone after the rapid infusion of an opioid is not known. Experimental animal study<sup>28</sup> indicated that stimulation of central mu<sub>1</sub> - opioid receptors increases efferent motor traffic, resulting in muscle contraction and rigidity. Additional data<sup>29</sup> demonstrate that whereas systemic opiate-induced muscle rigidity is primarily due to the activation of central mu receptors, supraspinal delta-1 and kappa-1 receptors may attenuate this effect.

Experimental studies in rats<sup>28,30</sup> based on combined physiologic, pharmacologic, histochemical, and immunocytochemical evaluations have demonstrated, that fentanyl may elicit muscular rigidity by activating spinal motoneurons by acting on the locus ceruleus in the pons. The locus ceruleus is the principal source of central nervous system norepinephrine. It appears that the participation of the cerulospinal noradrenergic pathway in fentanyl-induced muscular rigidity is critical<sup>28</sup>. In addition to the cerulospinal noradrenergic mechanism, the cerulospinal glutamatergic pathway and both NMDA and non-NMDA receptors in the spinal cord may mediate fentanyl-induced muscular rigidity in the rat<sup>30</sup>. Fentanyl-induced muscular rigidity may involve disinhibition of spinal motoneurons via an action of norepinephrine and glutamate on separate neuronal populations in the spinal cord<sup>30</sup>.

Our patient was diagnosed postoperatively with essential tremor which is one common neurological disease. From the pathophysiology of the disease there are altered concentrations of some biochemical markers in these patients<sup>31</sup>. They have reduced cerebrospinal fluid concentrations of gamma-aminobutyric acid (GABA), glycine, and serine, with a slight increase in glutamate. Also there are abnormalities on thalamic GABA<sub>A</sub> receptors. In specific regions increased concentrations of norepinephrine are also found in

patients with essential tremor: 5-folds in locus ceruleus and 2-folds in cerebellar cortex<sup>32,33</sup>. So it is possible that these abnormalities made the patient more vulnerable to fentanyl-induced rigidity even with an unusually low dose of opioid.

In summary, we presented and discussed the successful management of a case of muscle rigidity

induced by an unusually low dose of fentanyl as primary agent during induction of anesthesia. Opioid-induced muscle rigidity causing respiratory compromise should be readily recognized and treated by anesthetists.

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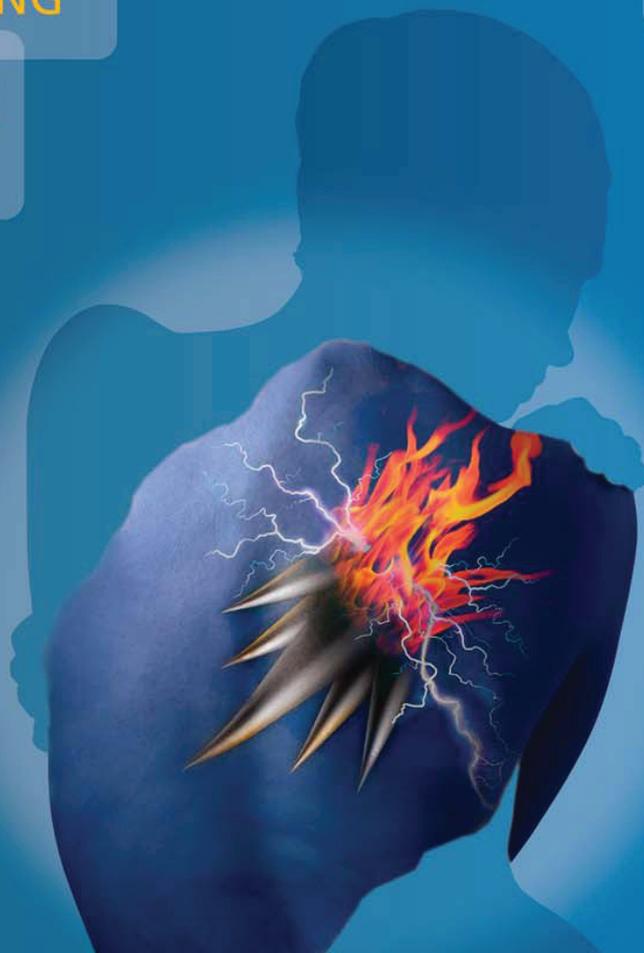
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<sup>†</sup> Train of four  
<sup>‡</sup> Post-tetanic counts  
<sup>§</sup> Second twitch

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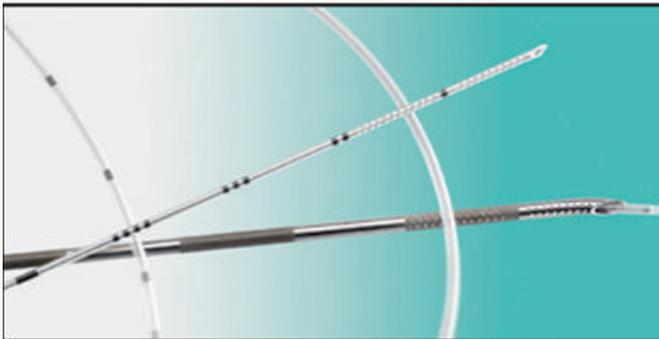
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