

CASE REPORT

Sedation in the ICU in myotonic dystrophy: a case report and review of the literature

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Keywords – Sedation, agitation, pharmacologic therapy, myotonic dystrophy**Abstract**

We present a case report of a patient with myotonic dystrophy, admitted to the intensive care unit after sternotomy for a mediastinal tumour. Because of prolonged weaning from ventilation and agitation, sedative medication was necessary. The usage of sedative drugs in patients with myotonic dystrophy is controversial, and they should be used with caution. We performed a review of the literature on sedation and agitation management in these patients. Literature describing anaesthesia and the direct postoperative care in myotonic dystrophy was found, but no literature on ICU management regarding sedation is available. While case reports suggest the dangers of sedative medications and opioids, the risks of these drugs are limited in intubated, ventilated and closely monitored patients.

Introduction

Myotonic dystrophy is the most common type of muscular dystrophy in adults.¹ It is a multisystem disease, inflicting problems in many organ systems. An increased rate of complications after elective surgery has been described,² including apnoea, atelectasis, pneumonia and sputum retention. These problems are related to pharyngo-oesophageal weakness, myotonia of the ventilatory muscles, an abnormal cerebral regulation of breathing,³ as well as a diminished vital capacity and chronic alveolar hypoventilation due to muscle weakness. Because of these problems, anaesthesia textbooks⁴ recommend to be careful with sedatives, muscle relaxants and opioids during anaesthesia. Recommendations for long-term sedation and pain management on the intensive care unit (ICU) are scarce.

We present a case report and our results of a literature review on ICU management regarding sedation in myotonic dystrophy. The patient's family gave written permission for publication of this report.

Case report

A 37-year-old female with myotonic dystrophy type 1 was scheduled for a thymectomy with removal of a mass, suspected to be lymphoma, in her mediastinum. The mass was detected eight years ago, but was managed conservatively because of the anticipated risks of surgery. However, continuing growth made removal necessary. The tumour, 16 x 15 x 3.5 cm in size, was removed after sternotomy. The phrenic nerves were identified and spared. The total duration of surgery was three hours. Postoperatively, she was admitted to our ICU. Initially, she was extubated 90 minutes after admission. Because of muscular weakness, non-invasive ventilation (NIV) was started on the first postoperative day. After 12 hours of NIV, progressive respiratory failure occurred and she was intubated again. A tension pneumothorax, possibly adding to the respiratory problems of the patient, was diagnosed and treated. On the 5th postoperative day she was extubated again, after which NIV was started immediately. Nevertheless, she required mechanical ventilation again on the 6th postoperative day because of sputum retention and atelectasis. Finally, on the 9th postoperative day she was successfully extubated and discharged to the ward five days later. A problem during her ICU stay was managing her anxiety and agitation, both when intubated, but also after extubation, because most sedative medications are considered to be contraindicated in myotonic dystrophy. In the end, we managed her anxiety and agitation when she was intubated with continuous administration of low dosage propofol (1.5 to 2.5 mg/kg/h) under monitoring of haemodynamic and respiratory parameters. This dosage was enough to keep the patient comfortable without experiencing any negative side effects. After extubation no sedatives were administered.

Methods

We performed a review of the literature, to find advice on sedation strategies in patients with myotonic dystrophy. We searched PubMed, used terms included myotonic dystrophy,

sedation, intensive care, anaesthesia, benzodiazepines, opioids, propofol, thiopental, fentanyl, morphine, remifentanyl, clonidine, dexmedetomidine, diazepam, midazolam and lorazepam. Several articles regarding anaesthesia were found, but we failed to find any articles on ICU management. A major difference between anaesthesia and ICU sedation is that anaesthesia is normally short term, only up to several hours. Another difference is that dosages used are unsuitable for long-term sedation, but apply for general anaesthesia. Here, we report the results found for anaesthesia in these patients. The manuscripts identified were all case reports or case series.

Results

Sedation

Thiopental

Several cases of apnoea after administration of thiopental have been reported, but in a series of 219 patients with myotonic dystrophy operated between 1961 and 1986, Mathieu et al. could not link any specific drug to respiratory problems. They concluded that the respiratory depression could very well be a common depressant effect of anaesthetic drugs, rather than a specific effect of thiopental.²

Propofol

Propofol was used as an intravenous anaesthetic in several cases. One case report describes a local myotonia in one arm following injection, with spontaneous relaxation after approximately 20 seconds, perhaps caused by the pain of injecting the propofol.⁵ Another case report mentions a myotonic state after induction with propofol, but intubation was easy without muscle relaxants and it resolved after introduction of isoflurane.⁶ Other manuscripts mentioned no problems with the use of propofol.

Benzodiazepines

Benzodiazepines are frequently used for sedation and management of agitation, but the use in patients with myotonic dystrophy has been associated with severe respiratory depression in two case reports. In one case, small doses of midazolam (0.25 mg twice) were used for sedation as an additive to epidural anaesthesia for an abdominal hysterectomy, after which the patient developed a PaCO₂ of 99 mmHg and loss of consciousness. This was totally reversible by one gift of flumazenil.⁷ Another case report describes a respiratory arrest in a previously undiagnosed patient undergoing an abdominal hysterectomy with intrathecal anaesthesia. She received additional sedation with diazepam 5 mg requiring mask ventilation. Postoperatively, this patient was diagnosed with myotonic dystrophy.⁸ However, both patients also received central neuraxial anaesthesia, which has been associated with a

decreased needed dosage of intravenous anaesthetics to reach a defined level of sedation. Therefore, these case findings cannot be extrapolated to patients not receiving central neuraxial anaesthesia.⁹

Analgesia

Remifentanyl

Remifentanyl is a short-acting opioid receptor antagonist, frequently used for sedation on the ICU. Based on its pharmacokinetic profile, with a predictable and short context-sensitive half-life, it is an attractive option, because dose adjustments have a fast clinical effect, and any respiratory depression could easily be handled by stopping the infusion. However, it is a very potent respiratory depressant, and there is no published experience with using remifentanyl for long-term sedation in patients with myotonic dystrophy. Safe usage of remifentanyl as part of general anaesthesia has been described in six case reports.¹⁰⁻¹⁵

A₂ adrenergic agonists

Clonidine and dexmedetomidine are agonists of central α_2 -adrenergic receptors, giving a sedative, analgesic, sympatholytic and anxiolytic effect, without significant respiratory depression in normal patients. Theoretically, they appear to be an interesting choice, but there is no published experience on the use of these drugs for long-term sedation in our patient group. The perioperative usage of dexmedetomidine in our patient group has only been described by Yoshino in a case report.¹⁶ The patient, who was scheduled for an abdominal hysterectomy with combined intrathecal and epidural anaesthesia, was sedated with dexmedetomidine. After initial administration of dexmedetomidine at 2 $\mu\text{g}/\text{kg}/\text{h}$, they observed an airway obstruction. After lowering the dosage, adequate sedation was achieved, and the authors concluded that dexmedetomidine should be carefully started at a low initial dose in patients with myotonic dystrophy.

Muscle relaxants

Succinylcholine has been associated with marked generalised contracture of skeletal muscles, but in Mathieu's series it was used without apparent adverse effects.² However, the author suggests it might be prudent to use short-acting non-depolarising muscle relaxants in these patients. Case reports document the safe use of atracurium and rocuronium.^{17,18} Sugammadex to antagonise a rocuronium-induced neuromuscular block has also been reported to be a safe option.^{11,19-22}

Discussion

Myotonic dystrophy is the most common type of muscular dystrophy in adults.¹ The estimated incidence is 1 in 8000 births, but a higher prevalence has been described. Myotonic dystrophy is caused by autosomal dominant nucleotide

repeat expansions, and it has two types. Type 1, also known as Steinert's disease, is the more severe variant, and has four subgroups: a congenital-onset, childhood-onset, adult-onset and a late-onset oligosymptomatic form. Adult onset is the most prevalent form. Type 2 has no distinct clinical subgroups, and only adult-onset forms have been described, but it can range from early adult-onset severe forms to very late-onset mild forms.

Adult-onset myotonic dystrophy type 1 disease shows multiorgan involvement, including muscle tissue, the heart, the brain and the endocrine system. It is characterised by adult-onset clinical myotonia, muscle weakness with disability by age 30-50, cataracts, cardiac conduction defects, tachyarrhythmias, behavioural changes and hypersomnia. Life expectancy is reduced. Muscle weakness in type 1 disease includes the facial muscles, distal limb muscles and the sternocleidomastoid muscle. Proximal limb, respiratory and bulbar muscle weakness is typically present later in life.

Type 2 disease shows clinical myotonia in less than 50% of patients. Cardiac conduction defects can range from absent to severe. Type 2 muscle weakness is usually less severe and typically develops later in life, bulbar weakness is not present, and respiratory weakness is only seen in rare cases.

An increased rate of complications after elective surgery has been described in type 1,² whereas the risk appears to be lower in type 2 disease.²³ Typical problems include apnoea, atelectasis, pneumonia and sputum retention. These problems are related to pharyngeal-oesophageal weakness, myotonia of the ventilatory muscles, an abnormal cerebral regulation of breathing,³ as well as a diminished vital capacity and chronic alveolar hypoventilation because of muscle weakness.

Given these problems, anaesthesia textbooks such as *Stoelting's Anesthesia and Co-Existing Disease*⁴ recommend to be careful with sedatives, muscle relaxants and opioids during anaesthesia, while *Uptodate* recommends avoiding general anaesthesia in type 1 disease whenever possible.²⁴ The disease characteristics of myotonic dystrophy will also lead to an increased risk of ICU treatment. It is therefore surprising that we did not find any articles documenting the usage of sedative medication in these patients in the ICU. The experience with sedative medication in anaesthesia cannot necessarily be extrapolated to usage in the ICU. The perioperative case reports suggest the dangers of sedative medications and opioids, but these drugs are in our opinion not contraindicated in the intubated and ventilated patient, and perhaps can also be used with due caution and appropriate monitoring in the spontaneously breathing patient. In general, we would recommend the use of short-acting sedatives, such as propofol, and to use only those sedatives one is familiar with.

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