MINERVA ANESTESIOL 2007;73:475-9

CASE REPORT

Anesthesia and myotonic dystrophy (Steinert's syndrome). The role of total intravenous anesthesia with propofol, cisatracurium and remifentanyl. Case report

V. CATENA [1], D. D. DEL MONTE [2], A. RUBINI [3], C. GUCCIONE [4], F. RICAGNA [4], G. GANGERI [4], G. F. DE ZEN [1]

[1]Intensive Care Unit, ULSS 3, Bassano del Grappa Hospital, Vicenza, Italy; [2]Intensive Care Unit, ULSS 15, Camposampiero Hospital, Padoa, Italy; [3]Institute of Human Physiology, University of Padoa, Padoa, Italy; [4]Department of Surgery, ULSS 3, Bassano del Grappa Hospital, Vicenza, Italy

ABSTRACT

Anesthesia for patients with Steinert's syndrome (myotonic dystrophy, MD) is a challenge for the anaesthetist. MD is a multisystemic disease and the neuromuscular symptoms can be associated with sleep apnea, endocrine disorders (diabetes, hypogonadism, hypothyroidism), cardiac, gastroenteric or cognitive disorders (mental deficiency, attention disorders). The diagnosis is facilitated when one or more of these symptoms are associated with the neuromuscular symptoms; however, the latter are not always present at the onset, which makes the diagnosis of MD a difficult and often late one. The choice of drugs and the choice of anesthesia in these patients can be very challenging for many reasons. A myotonic crisis can be triggered by several factors including hypothermia, shivering and mechanical or electrical stimulation. These patients are very sensitive to the usual anesthetics such as hypnotics and paralyzing agents (both depolarizing and nondepolarizing). The following case report describes pathophysiological considerations and a technique for anaesthesia during thoracic surgery that has been able to assure hemodynamic peroperative stability, early extubation and prolonged respiratory autonomy in a patient affected by this genetic disorder.

Key words: Myotonic dystrophy, diagnosis - Anesthesia - Myotonic dystrophy, therapy.

Myotonic dystrophy (MD) is a severe dominant autonomic multisystemic disorder with an incidence of 1/8000 newborns and a prevalence of 2.1-14.3/100 000.

The clinical picture of MD can range from an extremely severe often fatal congenital myopathy to a late onset form which usually presents after 50 years of age with a cataract as the only manifestation and has no impact on life expectancy.

In the classical presentation of MD the neuromuscular symptoms start to appear between the second and third decades of life. The clinical picture consists of myotonia (slow relaxation after contraction), progressive weakness and wasting of facial, respiratory, laryngeal, axial and distal limb muscles.

MD is also a multisystemic disease and the neuromuscular symptoms can be associated with sleep apnea, endocrine disorders (diabetes, hypogonadism, hypothyroidism), and cardiac, gastroen-

TABLE I.— *Hematic values before surgery.*

WG	RG	Hb (g/dL)	Ht%	Pts	Blood glucose (mg/dL)	Proteins (mg/dL)	INR	PTT (s)
17.5	3.59	11.5	34.9	440	135	5.6	1.09	49

WG: 10^3/μL; RG: 10^6/μL; Hb: hemoglobin; Plts: 10^3/μL platelets.

teric or cognitive disorders (mental deficiency, attention disorders). The diagnosis is facilitated when one or more of these symptoms are associated with the neuromuscular symptoms; however, the latter are not always present at the onset, which makes the diagnosis of MD a difficult and often late one.

The molecular genetic basis of MD is the presence of an instable trinucleotide (cytosine - timine - guanine, CTG) on chromosome 19. This is responsible for an impairment of the voltage-dependent membrane chloride channels in myocytes. A less common variant of muscular dystrophy involving proximal muscles (proximal myotonic myopathy, PROMM) is related to a repeated sequence (CCTG) on chromosome 3 and cannot be confused with the Steinert's syndrome.[1]

The choice of drugs and the conduct of anesthesia in these patients can be very challenging for many reasons. A myotonic crisis can be triggered by several factors including hypothermia, shivering and mechanical or electrical stimulation. These patients are very sensitive to the usual drugs used in anesthesia such as hypnotics and paralyzing agents (both depolarizing and nondepolarizing). The has been a report of hypersensitivity to neostigmine and a dubious response to halothane and the caffeine test, both of which are used to screen for malignant hyperthermia.

In the present case report, the authors propose an anesthesia technique that has been able to assure hemodynamic peroperative stability, early extubation and prolonged respiratory autonomy in a patient affected by this genetic disorder.

Case report

The patient is a 67 year old man, with a weigth of 65 kg and height of 168 cm and a previous diagnosis of MD, who was in need of emergency thoracoscopy or thoracotomy for respiratory failure and sepsis secondary to a right metapneumonic empyema (Table I).

His past medical history, in addition to MD, was remarkable for appendectomy (age 15), laminectomy (age 56 and 59), benign prostatic hypertrophy, nontoxic goiter and hyperglycemia.

At age 58 a permanent cardiac pace-maker was implanted for atrial conduction disease. His ability to walk had been progressively worsening to only 10 m other the previous few months. He was complaining of shortness of breath, dysphagia and dysphonia.

On clinical examination the patient was alert and oriented. There was dullness and absence of breath sounds in the right chest. Arterial blood oxygen saturation (SaO_2) was constantly less than 90% despite oxygen supplementation. The patient was on broad spectrum antibiotics for sepsis and mexiletin 200 mg *q.d.*

At the preoperative evaluation his general condition was considered so poor that he was classified as ASA 4.

The anesthesia team considered the full clinical picture a total intravenous anesthesia (TIVA) with propofol /remifentanyl drip and cisatracurium boluses.

Anesthesia was induced with propofol 1.5 mg/kg in a 120 s plus, remifentanyl 1.2 μg/kg in 60 s, and cisatracurium 0.2 mg/kg. The patient was mask ventilated for 2 min with 100% O_2 and subsequently intubated with a # 39 left double lumen tube.

Fiberoptic bronchoscopy was performed to assess the correct position of the bronchial limb of the orotracheal tube. Intraoperative analgesia and hypnosis were maintained by continuous infusion of remifentanyl (0.2±0.1 μg/kg/min) and propofol (4 mg/kg/h). Myorelaxation was assured through the operation by cisatracurium boluses (0.015 mg/kg q 30 min). Single lung ventilation with 100% O_2 was initiated before turning the patient in the thoracotomy position and was continued until lung inflation was necessary.

Video-assisted thoracic surgery (VATS) was performed, followed by right postero-lateral standard thoracotomy and open pleural decortication. The duration of the procedure was 4 h and 30 min (about 4 h of single lung ventilation). Hemodynamics were stable and normal through out the length of the procedure; the

hart rate was 60 bpm (sinus rhythm on D2) and invasive arterial blood pressure was 130/70 mmHg ±10 without pharmacological support. The lung was first inflated under direct vision and then full expansion was confirmed with a chest X-ray in the recovery room.

Local anaesthesia (levobupivacaine 0.35%) was used to block the intercostal nerves prior to closing the thoracotomy.

Once in the supine position, 60 min after the last dose of cisatracurium and 15 min after the remifentanyl/ propofol drip was stopped and after infusion of tramadol 1 mg/kg i.v., the patient was breathing spontaneously and was extubated without need for antagonizing the neuromuscular block.

The patient was kept under strict surveillance in the recovery room for about 1 h, under observation for early signs of muscular fatigue or respiratory distress. The patient was discharged to the surgical ward in good condition, fully awake with normal vital signs (respiratory rate 13 bpm, heart rate 87 bpm and arterial blood pressure 150/65 mmHg). Postoperative analgesia was assured in the first 48 h by continuous i.v. infusion of a analgesic cocktail (tramadol: 8.4 mg/h and ketorolac 1 mg/h).

The postoperative course was uneventful and the patient was discharged from the surgical ward on the 6th postoperative day.

Discussion

MD, first diagnosed by Steinert in 1909, represents a challenging anesthesiological problem because of the associated neuromuscular and systemic implications. Both MD and its proximal variety (PROMM) are secondary to mutations occurring respectively on chromosome 19 and 3, the same chromosomes involved in malignant hyperthermia. This peculiarity exposes the myotonic patients to the risk of developing this serious complication every time "trigger" medications, as succynilcholine or halogenated gases are used.

Follow-up studies in patients with MD show an incidence of mortality 7.3 times higher than patients without MD matched for age. Moreover, the life expectancy in these patients is 53 years, significantly shorter than the general population.

Pelargonio *et al.* [2] gave special consideration to the cardiac muscle and to the conduction tissue in MD patients. Autopsy specimens from patients deceased with MD and endomyocardial biopsies of patients with MD have shown endomyocardial fibrosis associated with fatty degeneration and hypertrophy of myocardial cells and focal myocarditis. Although neuromuscular impairment is the mainstay of the diagnosis, sometimes the onset of the disease can be mainly cardiac, presenting with atrial fibrillation, flutter, ventricular tachycardia or ventricular fibrillation.[3] Several authors suggest systematic electrophysiological studies in patients with a personal history of loss of consciousness or a family history of sudden death [4] with the purpose of discovering latent defects in the conduction tissue. On the other hand, ventricular tachycardia is inducible in only 18% of patients with MD and other electrophysiological abnormalities are rarely seen on dynamic EKG (Holter).[5]

Signs of cardiac ischemia are not easily appreciated in MD due to the scarcity of physical activity in these patients.

The Doppler echocardiographic assessment of left ventricular diastolic function has been able to demonstrate a myocardial equivalent of skeleton muscle myotonia.[6]

Considering the conduction abnormalities seen in MD, in particular when the HV interval is >70 ms, several authors advocate prophylactic implantation of a permanent pacemaker.[7]

The remarkable susceptibility of MD patients to anesthetic and sedative drugs and the fact that a myotonic crisis can be triggered by cold or shivering increases the risk of any surgical procedure, although major surgeries (such as thoracic surgery) proportionally increases both morbidity and mortality.

Dundee and Bourke underlined the susceptibility of MD patients to thiopental, which can frequently cause apnea and respiratory depression.[8, 9] Other authors have not been able to confirm these findings, such as in a retrospective study of 219 patients with MD undergoing different surgeries.[10]

There is also disagreement regarding the use of propofol.

Some authors report prolonged apnea and respiratory depression [11] while others have been able to carry out 3 h otorhinolaryngological anesthesia with propofol drip plus atracurium without problems.[12] Speedy advises a hypnotic dosage of 1 mg/kg of propofol without the need for curare for muscle relaxation, but confirms the prolonged awakening time.[13]

Tzabar *et al.* use target controlled infusion (TCI) of propofol in MD patients, starting with 12 μg/mL for intubation and followed by maintenance with a lower dose. They state that curare is not mandatory for intubation and confirm the prolongation of the awakening time even if their patients had muscular fatigue only.[14]

Others describe the combined use of propofol and atracurium for oral cavity surgery. They use propofol at a starting dose of 2.5 mg/kg followed by an infusion of 6 mg/kg/h, fentanyl 2 μg/kg, atracurium 0.5 mg/kg and 50% N_2O in oxygen.

They do not report any adverse effect with this technique.[15, 16]

The use of halogenated gases seems particularly contraindicated for many reasons. First, the relation between myotonia and malignant hyperthermia is unclear. Second, there is an increased potential for myocardial depression with this class of medications.[17] On the other hand, high doses of halogenated gases have been effective in interrupting myotonic status, although treatment may be followed by deep respiratory depression.

The same considerations apply to neuromuscular block in MD patients. Succynilcholine can trigger a myotonic crisis causing difficulties in orotracheal intubation and ventilation.[18, 19]

Nondepolarizing curares on the other hand, although eliciting a normal qualitative response, in patients with muscular deficit or weakness they cause a marked delay in muscular strength recovery. Because the marked sensitivity to acetylcholine, neostigmine should not be used to antagonize neuromuscolar block in myotonic patients,[20] although this drug has been used in some cases without adverse effects.[21] For all these reasons, the choice of a short-lived nondepolarizing curare that does not need antagonization seems logical. Owing to the specific pharmacodynamic and pharmacokinetic characteristics, mivacurium has been used first, followed by the atracurium and then by its cis isomer.[12, 16, 22, 23]

Cardiovascular and respiratory disturbances are common after surgery in MD patients, with an incidence as high as 38.1% [10] and reports of significant mortality and morbidity associated with this disease.

The respiratory pathophysiology of the patient with myotonic distropy is characteristic. The respiratory pattern described as " rapid shallow breathing" is pathognomonic of the disease and is related to the increasing elastic burden and increasing muscular weakness. The progressive reduction of the tidal volume causes a decrease of the afferent input from the periphery to the supraspinal centers, worsening the perception of shortness of breath.[24] Hypercapnia, a constant finding in these patients, is related to the stage of the disease and depends on restriction of lung volume (vital capacity) and weakness of respiratory muscles. A cause-effect relationship has been demonstrated between the increase in lung and respiratory elastance and impedence, and hypercapnia in severely impaired subjects. The increase in the respiratory apparatus elastance has been related to not only to respiratory muscle dystrophy but also to microatelectasies and chest wall deformity.[25] Patients with MD are not able to efficiently use the expiratory abdominal muscles to decrease the end-expiratory volume, which is one of the compensatory mechanisms in normal subjects during respiratory distress. Because several EMG studies of the abdominal muscles confirm the recruitment of motor units, this phenomenon is believed to be secondary not only to the impaired mechanical behavior of the chest wall but also to intrinsic muscular weakness. These peculiar changes in the respiratory pattern cause increased respiratory work which is observed in MD patients.[26, 27]

Thoracotomy by itself causes a 25% reduction in the vital capacity, greater than 50% reduction in chest wall compliance, a 149% increase of respiratory work and a 30% reduction of pressure generated with cough. Moreover, the incisional pain can trigger respiratory muscle dysfunction.[28, 29] For all these reasons, the use of short acting anesthetic drugs, permitting a rapid recovery of both consciousness and muscular strength, are indicated, provided that adequate analgesia is assured.

Conclusions

Considering the peculiar cardio-respiratory changes of Steinert's myotonic dystrophy, TIVA consisting of continuous infusion of short acting drugs such as propofol, remifentanyl and cis-atracurium [30-32] could assure a rapid recovery of

the preoperatory status of myotonic patients undergoing major surgery.

Adequacy of analgesia, regardless of how it is obtained, is mandatory because an increased work of breathing secondary to painful stimuli can precipitate in these patients the occurrence of overt respiratory failure.

References

1. Reilly MM, Hanna MG. Genetic neuromuscolar disease. J Neurol Neurosurg Psychiatry 2002;73 Suppl 2:12 -21.
2. Pelargonio G, Dello Russo A, Sanna T, De Martino G, Bellocci F. Myotonic dystrophy and heart. Heart 2002;88:665-70.
3. Hadian D, Loewe MR, Scott LR. Use of an insertable loop recorder in a myotonic dystrophy patient. J Cardiovasc Electrophysiol 2002;13:72-3.
4. Clarke NRA, Kelion AD, Nixon J, Hilton DH, Forfar JC. Does cytosine – timine – guanine (CTG) expansion size predict cardiac events and electrocardiographic progression in myotonic dystrophy? Heart 2001;86:411-6.
5. Lazarus A, Varin J, Ounnoughene Z, Radvanyi H, Junien C, Coste J *et al.* Relationship among electrophysiological finding and clinical status, heart function, and extent of DNA mutation in myotonic dystrophy. Circulation 1999;99:1041-6.
6. Fragola PV, Calo L, Luzi M, Mammarella A, Antonini G. Doppler echocardiographic assessment of left ventricular diastolic function in myotonic dystrophy. Cardiology 1997;88:498-502.
7. Lazarus A, Varini J, Duboc D. Final results of the French diagnostic pacemaker study in myotonic dystrophy. PACE 2000;25:599-605.
8. Dundee JW. Thiopentone in dystrophy myotonia. Curr Res Anesth Analg 1952;77:257-61.
9. Bourke TD, Zuck D. Thiopentone in dystrophya miotonya . Br J Anaesth 1957;29:35.
10. Mathieu J, Allard P, Gobeil G, Girard M, De Breekeleer M, Begin P. Anesthetic and surgical complications in 219 cases of myotonic dystrophy. Neurology 1997;49:1646-50.
11. Milligan KA. Propofol and dystrophya myotonica. Anaesthesia 1988;43:513-4.
12. White DA, Smyth DG. Continuous infusion of propofol in *dystrophya myotonica*. Can J Anaesth 1989;36:200-3.
13. Speedy H. Exaggerated physiological responses to propofol in myotonic dystrophy. Br J Anaesth 1990;64:110-2.
14. Tzabar Y, Marshall R. Myotonic dystrophy and target – controlled propofol – infusion. Br J Anaesth 1995;74:107-14.
15. Bouly A, Nathan N, Feiss P. Propofol in myotonic dystrophy. Anaesthesia 1991;46:705.
16. Bennun M, Goldstein B, Finkelsthein Y, Jedeikin R. Continuous propofol anaesthesia for patients with myotonic dystrophy. Br J Anesth 2000;85:407-9.
17. Russel SH, Hirsch NP. Anaesthesia and myotonia. Br J Anaesth 1994;72:210-6.
18. Azar I. The response of patients with neuromuscolar disorders to muscle relaxants: a review. Anesthesiology 1984;61:173-87.
19. Aldridge LM. Anaesthetic problems in myotonic dystrophy. Br J Anesth 1985;57:1119-30.
20. Buzello W, Krieg N, Schlickewei A. Hazards of neostigmine in patients with neuromuscolar disorders . Report of two cases. Br J Anaesth 1982;54:529-34.
21. Drachman DB, Fambrough DM. Are muscle fibers denervated in myiotonic dystrophy? Arch Neurol 1976;33:485-8.
22. Nightingale P, Healy TE, McGuinness K. *Dystrophya myotonica* and atracurium. A case report. Br J Anaesth 1985;57:1131-5.
23. Watt NA, Scott RPF. Mivacurium chloride and myotonic dystrophy. Br J Anaesth 1995;75:498-9.
24. Lanini B, Misuri G, Gigliotti F, Randelli I, Pizzi A, Romagnoli I et al. Perception of dyspnea in patients with neuromuscolar disease. Chest 2001;120:402-8.
25. Rimmer KP, Golar SD, Lee MA, Whitelaw WA. Myotonia of the respiratory muscles in myotonic dystrophy. Am Rev Respir Dis 1993;148(4 Pt 1):1018-22.
26. Begin P, Mathieu J, Almirall J, Grassino A. Relationship between chronic hypercapnia and inspiratory-muscle weakness in myotonic dystrophy. Am J Respir Crit Care Med 1997;156:133-9.
27. Ugalde V, Walsh S, Abresch TR, Bonekat HW, Breslin E. Respiratory abdominal muscle recruitment and chest wall motion in myotonic dystrophy. J Appl Physiol 2001;91:395-407.
28. Batras V, Kane G, Weibel S. Preoperative evaluation of patients with lung cancer undergoing thoracic surgery. Clin Pulm Med 2002;9:46-52.
29. Vassilakopoulos T, Mastora Z, Katsaounou P, Doukas G, Klimopoulos S, Roussos C *et al.* Contribution of pain to inspiratory muscle dysfunction after upper abdominal surgery. Am J Respir Crit Care Med 2000;161:1372-5.
30. Ornstein E, Lien CA, Matteo R, Ostapkovic ND, Diaz J, Wolf KB. Pharmacodinamic and pharmacokinetics of Cisatracurium in geriatric surgical patients. Anesthesiology 1996;84:520-5.
31. Glass PSA, Tong TJ, Howell S. A review of the pharmacocinetics and pharmacodynamics of remifentanil. Anaesth Analg 1999; 89 Suppl 4:S7-14.
32. Nishi M, Itoh H, Tsubokawa T, Taniguchi T, Yamamoto K. Effective doses of vecuronium in a patient with myotonic didtrophy. Anaesthesia 2004;59:1216-8.

Aknowledgments.—The authors would to thank our nurses for their qualified technical assistance.

Received on April 20, 2005 - Accepted for publication on June 27, 2007.

Address reprint requests to: V. Catena, Piazza Vittoria 30, 35010 Villa del Conte (PD), Italy. E-mail: vincenzocatena @ libero.it