

CAS CLINIQUE/CASE REPORT

USE OF REMIFENTANIL AND PROPOFOL WITHOUT MUSCLE RELAXANT COMBINED WITH INTRATHECAL MORPHINE IN CHILDREN WITH DUCHENNE'S MUSCULAR DYSTROPHY UNDERGOING SPINAL SURGERY

<http://www.lebanesemedicaljournal.org/articles/56-3/case1.pdf>

Freda RICHA, Alexandre YAZIGI, Patricia YAZBECK*

Richa F, Yazigi A, Yazbeck P. Use of remifentanyl and propofol without muscle relaxant combined with intrathecal morphine in children with Duchenne's muscular dystrophy undergoing spinal surgery. *J Med Liban* 2008 ; 56 (3) : 181-184.

ABSTRACT : Duchenne's muscular dystrophy (DMD) is the most common and severe form of myopathy occurring in pediatric patients. Sensitivity of patients with DMD to sedative, anesthetic and neuromuscular blocking agents may result in intraoperative and early postoperative cardiovascular and respiratory complications, as well as prolonged recovery from anesthesia. Anesthetic management of these patients is challenging and may cause serious problems to the anesthesiologist. We report the use of a total intravenous anesthesia technique (TIVA) with remifentanyl and propofol without muscle relaxants, associated with intrathecal morphine in three children with DMD undergoing posterior spinal surgery (PSS). Tracheal intubation was successfully done with good conditions. The intraoperative course of these patients was uneventful. Controlled hypotension, rapid recovery and uneventful postoperative period were achieved with this technique.

In conclusion, good conditions for tracheal intubation, controlled hypotension, rapid recovery and uneventful postoperative period can be achieved with this anesthesia technique in patients with DMD.

INTRODUCTION

Duchenne's muscular dystrophy (DMD) is the most common and severe form of myopathy occurring in pediatric patient [1]. DMD is an inherited disorder characterized by severe proximal muscle weakness, progressive degeneration, fatty infiltration of the muscles, and gradual motor function deterioration [2]. Children who have DMD were considered to be at high risk of perioperative cardiac and pulmonary complications. Specific anesthetic complications in persons with DMD are related to administration of succinylcholine and volatile anesthetics and

Richa F, Yazigi A, Yazbeck P. Usage du rémifentanyl et du propofol sans myorelaxants, avec morphine intrathécale dans la chirurgie du rachis chez les enfants atteints de dystrophie musculaire de Duchenne. *J Med Liban* 2008 ; 56 (3) : 181-184.

RÉSUMÉ : La sensibilité des patients atteints de dystrophie musculaire de Duchenne (DMD) aux sédatifs, anesthésiques et curares non dépolarisants (CND) peut entraîner des complications per opératoires et/ou cardiovasculaires et respiratoires postopératoires, aussi bien qu'un retard de réveil anesthésique. L'anesthésie de ces patients peut causer de sérieux problèmes aux anesthésistes. Nous rapportons l'usage de l'anesthésie intraveineuse totale (TIVA) avec rémifentanyl et propofol sans myorelaxants, associée à la morphine intrathécale chez trois enfants atteints de DMD, programmés pour une chirurgie réparatrice de scoliose par abord postérieur. L'intubation trachéale est réussie dans de bonnes conditions. Les périodes per et postopératoires sont sans incident notable. Une hypotension contrôlée et un réveil anesthésique rapide sont achevés avec cette technique.

En conclusion, la TIVA au rémifentanyl et propofol associée à la morphine intrathécale assure de bonnes conditions pour l'intubation trachéale, une hypotension contrôlée et un réveil anesthésique rapide chez les enfants avec DMD sans incident postopératoire notable.

included cardiac arrhythmias, cardiac arrest and a malignant hyperpyrexia-like syndrome [3-5]. There are also reports about the increased sensitivity of patients with DMD to non-depolarizing neuromuscular blocking agents (NMBA) [1-2]. Anesthetic management of these patients is challenging and may cause serious problems to the anesthesiologist. Therefore, the anesthetic drugs must be carefully selected.

We report in this paper the use of an anesthetic regimen based on a total intravenous anesthesia technique (TIVA) with remifentanyl and propofol without NMBA associated with intrathecal morphine in three children with DMD undergoing posterior spinal surgery (PSS).

CASE REPORTS

Three male patients with DMD, wheelchair-dependent, aged 10, 11 and 13 years respectively, were admitted to our department for posterior spinal surgery correction. The patients showed a decreased in pulmonary function

*Department of Anesthesia and Intensive Care, Hôtel-Dieu de France Hospital, Saint-Joseph University, Beirut, Lebanon.

Correspondence : Freda RICHA, MD. Hôtel-Dieu de France Hospital. Anesthesia and Intensive Care Dept. Alfred Naccache Street. POBox 166830 Ashrafieh-Beirut. Lebanon.

Tel : +961 3 872077 Fax : +961 1 615295

e-mail : fredrich24@yahoo.com OR fredrich8@hotmail.com

TABLE I
PATIENTS' DEMOGRAPHIC
AND RELEVANT SURGICAL DATA

	Patient 1	Patient 2	Patient 3
AGE (yr)	10	11	13
WEIGHT (kg)	31	35	38
FVC (% predicted value)	57	54	50
FEV1 (% predicted value)	65	63	59
PRE-OPERATIVE CK (U/L)	3340	4270	3280
CARDIOMYOPATHY	-	+	-
SURGICAL TIME (min)	380	335	320
RECOVERY TIME (min)	12	9	10
LOWEST POSTOPERATIVE SpO ₂ (%)	96	98	94

FVC : forced vital capacity FEV1 : forced expiratory volume in 1 s
CK : creatine kinase

tests and elevated creatine kinase (CK). One patient (Pt 2) showed cardiomyopathy with 45% of left ventricular ejection fraction on echocardiography. Patients' characteristics are presented in table I.

Institutional approval and parental informed consent were obtained for the three children. The patients were premedicated with 1 mg/kg of hydroxyzine (Atarax®) administered orally one hour before the induction of anesthesia. In the operating room, routine monitoring including 5 leads ECG, pulse oxymeter, non-invasive blood pressure measurement and an IV line were started. End-tidal CO₂ concentration was also recorded from the time of anesthesia induction to the time of extubation. The anesthesia machine was prepared by using a disposable circuit, a fresh CO₂-absorbent, disconnecting the vaporizers and flushing with O₂ at a rate of 10 l/min for 20 minutes before use. Continuous assessment of the depth of anesthesia and level of consciousness was achieved according to the Bispectral Index Scale (BIS) using the electro-encephalographic electrodes (with BIS 0 = cortical silence, BIS 100 = awake ; whereas BIS values of 45-65 are recommended for deep general anesthesia).

General anesthesia was induced with remifentanyl infusion 1 µg/kg/min for 1 min during which the patient was pre-oxygenated followed by propofol 3-5 mg/kg without neuromuscular blocking agents. Laryngoscopy and intubation were performed easily. Mechanical ventilation with 40% oxygen and 60% nitrous oxide was begun. The patients were placed in the lateral decubitus position, lumbar puncture was performed, under sterile conditions, with a 90 mm 25 gauge pencil point needle between L4-L5 interspace. A single-dose of morphine 4 µg/kg was administered intrathecally to provide postoperative analgesia. The patients' conditions were monitored continuously by routine monitoring and a radial arterial catheter, an end-tidal CO₂ (ETCO₂ maintained between 35-40 mmHg), a rectal temperature (T°) probe (T° maintained between 36°C and 37°C) and BIS. The surgery was performed in the prone position. The posterior instrumentation of the spine

was done with pedicle screws in the thoracic and lumbar spine. The procedures were performed over a minimum of seven or maximum of eleven vertebral levels. Anesthesia was maintained with continuous infusion of remifentanyl 0.1 to 0.4 µg/kg/min to provide a systolic arterial pressure (SAP) close to 80 mmHg and propofol 3 to 9 mg/kg/h to provide a target BIS index between 40 and 50. Volatile anesthetics were not used.

Monitoring of posterior spinal cord function was assessed by the wake-up test performed at the surgeon's request. Then the infusion of propofol and remifentanyl was stopped. The BIS was helpful in the continuous assessment of the waking process. BIS increased from the 40's to the 80's in 9 to 12 min after discontinuation of drugs and nitrous oxide during the test. Patients were asked repeatedly during the wake-up test, at least every 30 s, to open their eyes and to move their hands and feet. After finishing the wake-up test, maintenance of anesthesia was continued, as previously described.

Blood loss was adequately corrected by transfusion of packed red blood cells. Hemoglobin was maintained between 9 and 11 g/dl. On completion of surgery, the patients were extubated in the operating room after regaining consciousness and fulfilling the extubation criteria. The patients were then transferred to the pediatric intensive care unit for 24 hours. The intraoperative course of these patients was uneventful. HR and SAP measured at key points intraoperatively are presented in figure 1. Mean highest and lowest HR were 75 ± 5 and 60 ± 3 beats/min. Mean highest and lowest SAP were 92 ± 10 and 78 ± 6 mmHg. Lowest postoperative SpO₂ was 96 ± 2 %. The surgical times were respectively 380, 335 and 320 minutes (mean duration was 345 ± 31 min). The recovery times (from the end of surgery to extubation) were respectively 12, 9 and 10 minutes (mean recovery time was 10.33 ± 1.53 min).

Postoperative pain was assessed at 2-h intervals by means of a VAS from 0-100 (where 0 = no pain ; 100 = the worst pain imaginable). All patients received intravenous paracetamol 15 mg/kg every 6 h. As a rescue analgesic, intravenous morphine 0.02 mg/kg was administered if VAS was greater than 30 and titrated to keep a respiratory rate greater than 10 breaths/min. No patient needed rescue analgesic the first 18 hours postoperatively. There was no nausea and vomiting, nor cardiac or respiratory complications postoperatively.

DISCUSSION

Anesthetic management of patients with DMD is challenging and may cause serious problems to the anesthesiologist. Because of the marked sensitivity of these patients to sedatives and anesthetic agents and the increased risk of precipitating rhabdomyolysis or malignant hyperthermia by anesthetic drugs [1, 2, 6], the safest anesthetic technique has still to be established. As a possible association between malignant hyperthermia and DMD has been documented, our anesthetic technique was administered with-

out triggering agents. Due to the two particularities of the spinal surgery (controlled hypotension avoiding excessive intraoperative bleeding and intraoperative wake-up test) we used an anesthetic protocol based on propofol and remifentanyl without myorelaxant or volatile anesthetics, in three children undergoing posterior spinal surgery. We recommend remifentanyl for children with DMD. Its potency and its rapid onset of action have potentiated the anesthesia, decreased the risk of intraoperative awareness and blunted the hemodynamic changes associated with laryngoscopy and surgery (Fig. 1). Because remifentanyl's metabolism is independent of liver and renal function, our patients benefited from its analgesic properties without the risk of drug accumulation. In addition, remifentanyl's short duration of action prevented prolonged postoperative respiratory depression and sedation. We found the combination of propofol and remifentanyl infusions with nitrous oxide in oxygen to be successful for patients with DMD undergoing spinal surgery. Exaggerated reactions to drugs were not observed. Intraoperative BP and HR were stable and the wake-up test was successful. The recovery period was smooth and relatively short, less than 12 min. There were no serious postoperative respiratory or cardiac complications. The stable intraoperative period, uneventful recovery and lack of postoperative complications in our report may be explained by the following factors : First, the use of ultra-short agents (propofol and remifentanyl) for anesthesia ; secondly, the use of a BIS monitoring during the operation which was maintained between 40 and 50 helping to titrate the anesthetic drugs and avoiding intraoperative awareness or over-dosage of

propofol ; third, the avoidance of the use of NMBA ; fourth, the avoidance of succinylcholine and volatile anesthetics.

Several complications in association with general anesthesia have been reported in patients with DMD. They were almost exclusively related to the use of succinylcholine and to inhalational agents [7-8]. There is no variable which preoperatively identifies patients who will develop complications during anesthesia [9]. Succinylcholine is contraindicated because of the risks of rigidity, rhabdomyolysis, myoglobinuria, malignant hyperthermia, hyperkalemia, and cardiac arrest [3-4, 6-8]. In contrast, non-depolarizing neuromuscular blocking drugs usually evoked a normal response. However, if muscle wasting exists, a prolonged response may occur necessitating the reversal of the muscle relaxant [10-11]. The anticholinesterase drugs used to reverse neuromuscular blockade may precipitate rhabdomyolysis in these patients [12]. Inhalational agents may be deleterious in patients suffering from muscular dystrophy and should be used with caution. Volatile anesthetics can act to disrupt cellular membranes leading to rhabdomyolysis and hyperkalemia in rare cases of DMD [13-16].

Capozzoli et al. [17] have reported the case of a 3-year-old child, affected by DMD and undergoing adenoidectomy and bilateral myringotomy, who received total intravenous anesthesia (propofol infusion 160 mcg/kg/min and remifentanyl 0.55 mcg/kg/min) without any muscle relaxant. The postoperative period was uneventful. Cossu et al. [18] reported the case of a 11-year-old patient with DMD who received general anesthesia with propofol in con-

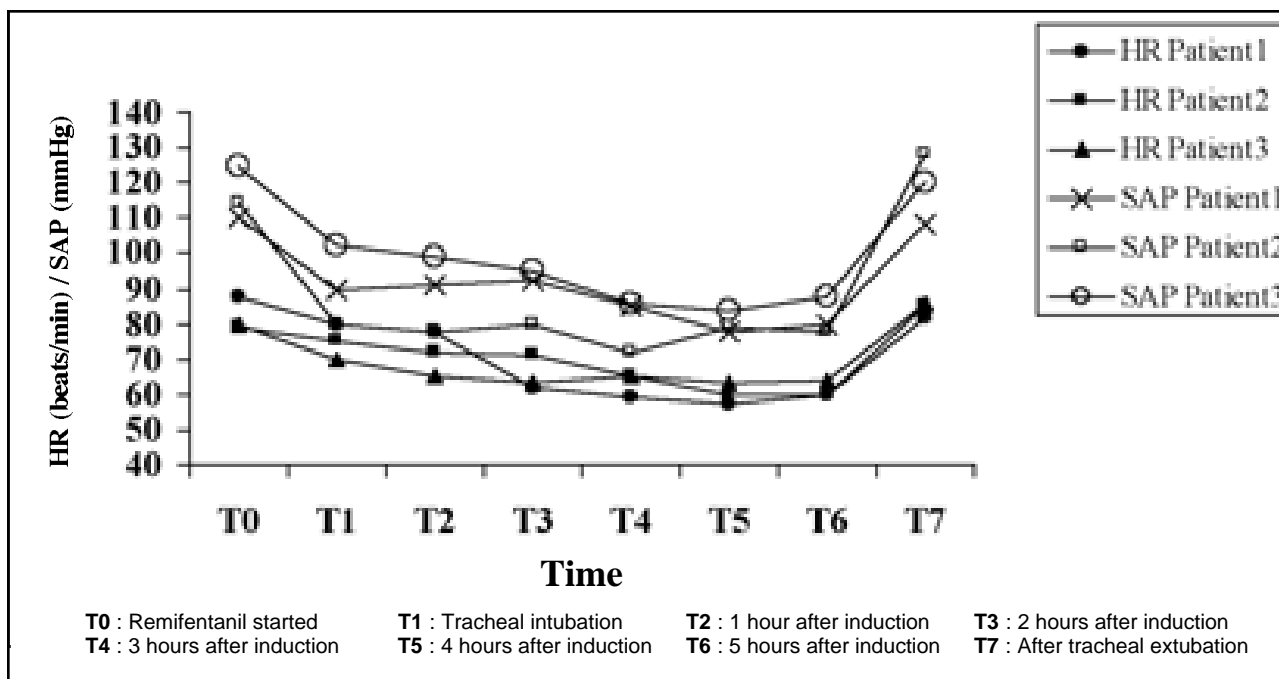


FIGURE 1
Intraoperative heart rate and arterial blood pressure variations during general anesthesia with remifentanyl and propofol in three children with DMD undergoing posterior spinal surgery

tinuous infusion, fentanyl and nitrous oxide in oxygen without any myorelaxant. This anesthesia technique proved to be safe and easy, allowing a rapid postoperative recovery without any cardiovascular complication.

Intrathecal morphine was successfully used in these patients for postoperative analgesia without any need for rescue analgesics during the first 18 hours postoperatively. Sethna et al. [19] have published about postoperative pain management, after upper abdominal procedures, in an adolescent with DMD, progressive spinal scoliosis and poor pulmonary function. A combined technique of subarachnoid and general anesthesia was used during surgery. Postoperative administration of small intermittent doses of subarachnoid morphine produced profound analgesia, which eliminated the need for systemic opioids, restored preoperative arterial oxygenation within 48 hours after the operation, and expedited postoperative recovery.

In conclusion, the combination of propofol and remifentanyl infusions appears to be a suitable anesthetic technique for patients with DMD undergoing posterior spinal surgery. This total intravenous anesthesia technique without NMBA provides good conditions for tracheal intubation, controlled hypotension, wake-up test and rapid recovery from anesthesia. Further studies are required to evaluate this anesthetic technique in patients suffering from DMD undergoing different types of surgery including major abdominal or thoracic surgery.

REFERENCES

1. Frankowsky GA, Johnson JO, Tobias JD. Rapacurium administration to two children with Duchenne's muscular dystrophy. *Anesth Analg* 2000 ; 91 : 27-8.
2. Ririe DG, Shapiro F, Sethna NF. Response of patients with Duchenne's muscular dystrophy to neuromuscular blockade with vecuronium. *Anesthesiology* 1998 ; 88 : 351-4.
3. Larach MG, Rosenberg H, Gronert GA, Allen GC. Hyperkalemic cardiac arrest during anesthesia in infants and children with occult myopathies. *Clin Pediatr* 1997 ; 36 : 9-16.
4. Sullivan M, Thompson WK, Hill GD. Succinylcholine-induced cardiac arrest in children with undiagnosed myopathy. *Can J Anaesth* 1994 ; 41 : 497-501.
5. Sethna NF, Rockoff MA. Cardiac arrest following inhalation induction of anaesthesia in a child with Duchenne's muscular dystrophy. *Can Anaesth Soc J* 1986 ; 33 : 799-802.
6. Morris P. Problems posed for the anesthetist by Duchenne's muscular dystrophy. *Ann Fr Anesth Réanim* 1998 ; 17 : fi 102-4.
7. Larsen UT, Juhl B, Hein-Sorensen O, de Fine O. Complications during anaesthesia in patients with Duchenne's muscular dystrophy (a retrospective study). *Can J Anaesth* 1989 ; 36 : 418-22.
8. Breucking E, Reimnitz P, Schara U, Mortier W. Anesthetic complications. The incidence of severe anesthetic complications in patients and families with progressive muscular dystrophy of the Duchenne and Becker types. *Anaesthesist* 2000 ; 49 : 187-95.
9. Sethna NF, Rockoff MA, Worthen HM, Rosnow JM. Anesthesia-related complications in children with Duchenne's muscular dystrophy. *Anesthesiology* 1988 ; 68 : 462-5.
10. Schmidt J, Muenster T, Wick S, Forst J, Schmidt HJ. Onset and duration of mivacurium-induced neuromuscular block in patients with Duchenne's muscular dystrophy. *Br J Anaesth* 2005 ; 95 : 769-72.
11. Uslu M, Mellinghoff H, Diefenbach C. Mivacurium for muscle relaxation in a child with Duchenne's muscular dystrophy. *Anesth Analg* 1999 ; 89 : 340-1.
12. Buzello W, Kreig N, Schlickewei A. Hazards of neostigmine in patients with neuromuscular disorders. *Br J Anaesth* 1982 ; 54 : 529-34.
13. Takahashi H. Sevoflurane can induce rhabdomyolysis in Duchenne's muscular dystrophy. *Masui* 2002 ; 51 : 190-2.
14. Goresky GV, Cox RG. Inhalational anesthetics and Duchenne's muscular dystrophy. *Can J Anaesth* 1999 ; 46 : 525-8.
15. Smelt WL. Cardiac arrest during desflurane anaesthesia in a patient with Duchenne's muscular dystrophy. *Acta Anaesthesiol Scand* 2005 ; 49 : 268-9.
16. Obata R, Yasumi Y, Suzuki A, Nakajima Y, Sato S. Rhabdomyolysis in association with Duchenne's muscular dystrophy. *Can J Anaesth* 1999 ; 46 : 564-6.
17. Capozzoli G, Auricchio F, Accinelli G. Total intravenous anaesthesia without muscle relaxants in a child with diagnosed Duchenne's muscular dystrophy. *Minerva Anesthesiol* 2000 ; 66 : 839-40.
18. Cossu F, Caboni MT. Propofol in Duchenne's muscular dystrophy. *Minerva Anesthesiol* 1995 ; 61 : 51-3.
19. Sethna NF, Berde CB. Continuous subarachnoid analgesia in two adolescents with severe scoliosis and impaired pulmonary function. *Reg Anesth* 1991 ; 16 : 333-6.

إستعمال ريمييفنتانيل وبروبوفول بدون مرخي العضلات وبالاشتراك مع المورفين تحت الجافية (داخل الغلاف) عند الاطفال المصابين بحثل (اضطراب اغتذائي) عضلي، مرض "دوشين" وستجري لهم عملية جراحية .

موجز : حساسية الاطفال المصابين بالحثل العضلي "دوشين" لمهدئات التخدير والكورار اللا مستقطب قد تؤدي الى اختلاطات خلال المداخلة الجراحية و / أو قلبية عرقية وتنفسية بعد العملية وتأخر الاستيقاظ من التخدير. قد يؤدي تخدير هؤلاء المرضى الى مشاكل هامة . نشير هنا الى استعمال التخدير الوريدي العام بالريمييفنتانيل وبروبوفول بدون مرخي العضلات ولكن بالاشتراك مع المورفين تحت الجافية لثلاثة اطفال مصابين بداء دوشين لاجراء عملية جراحية بالشق الخلفي (اصلاح الجنبف، التواء العمود الفقري) . نجح التنبيب الرغامى بأسلوب جيد. تمت مراحل العملية وما بعدها بدون عوارض هامة . هبوط الضغط المراقب واستيقاظ سريع من التخدير تم وانتهت العملية بهذه التقنية من التخدير.

الخلاصة : ان التخدير العام بهذه الطريقة يؤمن شروطا جيدة للتنبيب الرغامى ومراقبة هبوط الضغط والاستيقاظ السريع من التخدير بدون حدوث يذكر تال للعملية.