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Case Report

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Combined General and Regional Anesthesia for a Patient With Duchenne Muscle Dystrophy With an Implanted Left Ventricular Assisted Device Undergoing Orthopedic Surgery

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Abstract

Duchenne muscular dystrophy (DMD) is an X-linked inherited dystrophinopathy, with an incidence of 1 in 3,600 - 5,000 male live-born infants. The leading cause of death is often cardiomyopathy-related heart failure. Given the progressive nature of the disorder with involvement of skeletal muscle, respiratory and cardiac function, perioperative care remains challenging with an increased incidence of perioperative morbidity and mortality. Perioperative care can be challenging due to life-threatening perioperative adverse events related to associated end-organ effects, as well as sensitivity to various anesthetic agents, rhabdomyolysis, hyperkalemia, hyperthermia, and cardiac arrest. We present a 22-year-old DMD patient with left ventricular assisted device (LVAD), who presented for repair of both left distal femur and tibial diaphysis fractures. Anesthetic care included the unique combination of total intravenous anesthesia with dexmedetomidine and remimazolam combined with regional anesthesia including a supra-inguinal fascia iliaca block, saphenous nerve block, and popliteal nerve block. The basics of dystrophinopathies are presented, perioperative concerns discussed, and previous reports of the use of regional anesthesia as an adjunct to general anesthesia in adult and pediatric patients with DMD are reviewed.

Keywords: Regional anesthesia; Duchenne muscular dystrophy; Left ventricular assisted device; Cardiomyopathy

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Introduction

Duchenne muscular dystrophy (DMD) is an X-linked recessive genetic disorder related to mutations in the dystrophin gene [1]. In muscle cells, the dystrophin complex localizes at the membrane and connects intercellular cytoskeleton to extracellular matrix [2]. The dystrophin complex acts as a membrane stabilizer during muscle contraction to prevent contraction-induced damage. Dysfunction of the dystrophin complex leads to progressive muscle damage and loss. DMD is typically diagnosed when a child fails to meet gross motor milestones during the first 10 years of life, frequently beginning as early as 2 years of age. As the muscles around the pelvis and thighs (proximal muscles) are affected first, the child often presents with difficulty managing stairs or assuming a standing position from sitting. By adolescence, patients generally loss their ability to ambulate independently and are usually wheelchair bound. In addition to its impact on the function of skeletal muscle, dysfunction of the dystrophin complex leads to progressive effects on myocardial function and eventual development of cardiomyopathy characterized by a progressive decline in ejection fraction, which generally becomes clinically evidence during the teenage years or early adult life [3, 4]. Following improvements in the management of respiratory dysfunction and insufficiency in these patients, cardiomyopathy has now become the leading cause of death. Given the associated respiratory and cardiac involvement as well as the cellular dysfunction of muscle cells, these patients have an exaggerated risk of morbidity and mortality during perioperative care.

We present a 22-year-old DMD patient with left ventricular assist device (LVAD), who presented for repair of left distal femur and tibial diaphysis fractures. The planned orthopedic procedures were left antegrade femoral nail and percutaneous screw fixation of the distal femur and tibia. The basics of dystrophinopathies are presented, perioperative concerns discussed, and previous reports of the use of regional anesthesia as an adjunct to general anesthesia in adult and pediatric patients with DMD are reviewed.

Review of this case and presentation in this format followed the guidelines of the Institutional Review Board at Nationwide Children's Hospital (Columbus, OH, USA).

Case Report

Investigations

A 22-year-old young adult male, weight 63.3 kg, height 155.7 cm, and body mass index (BMI) of 26.37 kg/m^2, with a history of DMD, presented for surgical repair of non-displaced fractures of the left distal femur and tibia, sustained following a fall. The patient was diagnosed with intermediate phenotype dystrophinopathy due to deletion of exon 51 of the *DMD* gene at the age of 5 years. He had developed severe left ventricular (LV) dysfunction and 1 year ago required placement of an LVAD (HeartMate 3, Abbott Cardiovascular). Additional past medical history included nocturnal biphasic positive airway pressure (BiPAP) dependence (inhalation positive/exhalation positive airway pressure (IPAP/EPAP) = 14/8 cm H_2O), short stature, and vitamin D deficiency. He had no known allergies. Because of the indwelling LVAD, he was receiving chronic anticoagulant therapy with oral warfarin. Additional medications included sacubitril/valsartan (49/51 mg) tablet (one tablet twice per day), eplerenone 50 mg tablet (one tablet once a day), metoprolol succinate extended release 25 mg tablet (one tablet per day), furosemide 20 mg tablet (0.5 tablet every 48 h as needed), warfarin 5 mg tablet (one tablet, 5 days a week and half a tablet 2 days a week), aspirin 325 mg tablet (one tablet every morning), metformin extended release 500 mg tablet (one table per day), dapagliflozin propanediol 10 mg tablet (one tablet per day), cholecalciferol 50 µg tablet (one tablet per day), calcium carbonate 600 mg-vitamin D3 10 µg (400 IU) tablet (two tablets once a day), sertraline 50 mg tablet (one tablet at bedtime), gabapentin 300 mg capsule (one tablet at bedtime), famotidine 20 mg tablet (one tablet twice daily), and biotin 10 mg tablet (once daily).

Diagnosis and treatment

Three days before the planned procedure, dapagliflozin, acetylsalicylic acid (ASA), and warfarin were held. Enoxaparin sodium 60 mg was started subcutaneously twice daily as bridging therapy for anticoagulation. The patient was scheduled for an elective left antegrade femoral nail and percutaneous screw fixation of both intraarticular distal femur and left distal tibia. Preoperative laboratory evaluation including a complete blood count, electrolytes, and renal function were normal. The hemoglobin was 15.9 g/dL with a hematocrit of 49.3%. The electrocardiogram showed sinus tachycardia (ventricular rate 120 beats/min), a shortened PR interval (92 ms), premature atrial complexes with aberrant conduction, and left axis deviation. The echocardiogram showed severely diminished biventricular systolic function, severe dilatation of the left ventricle, moderate dilatation of the right ventricle, mild mitral/aortic regurgitation, moderate tricuspid regurgitation, and no pericardial effusion. The LVAD was in place from the left ventricle to the proximal ascending aorta. The anesthesia plan included total intravenous anesthesia (TIVA) combined with regional blockade including a supra-inguinal fascia iliaca (SIFI), saphenous nerve (SN), and popliteal nerve (PN) blockade. The patient was held *nil per os* for 8 h and was transported to operating room where routine American Society of Anesthesiologists' monitors were applied. Anesthesia was induced with midazolam (4 mg) in two divided doses, etomidate (16 mg), and hydromorphone (1 mg) in two divided doses. Post-induction hypotension was treated with a single dose of phenylephrine (100 µg). Neuromuscular blockade was provided by rocuronium (70 mg). The patient's trachea was intubated with 7.0-mm cuffed endotracheal tube on the first attempt using a Macintosh 3 laryngoscope blade. An arterial cannula was inserted in the right radial artery (20 G) under aseptic technique. Maintenance anesthesia included dexmedetomidine at 1.5 µg/kg/h and remimazolam at 15 µg/kg/min. While the patient was in supine position, three single shots peripheral nerve blocks were performed with a total of 40 mL of 0.5% ropivacaine with dexamethasone 0.2 mg/mL and epinephrine 1:200,000 (15 mL for SIFI, 15 mL for PN, and 10 mL for SN). Cefazolin was administered for prophylaxis against a surgical site infection. There was no hemodynamic response to surgical incision. No intraoperative concerns were encountered. The LVAD was continued at the same settings throughout the perioperative period (5,200 revolutions per minute (RPM) with a cardiac output of 4 L per minute). The procedure lasted for 3.5 h. Total fluid administered during the procedure included crystalloid (250 mL) and albumin 5% (500 mL). At completion of the procedure, residual neuromuscular blockade was reversed with sugammadex (200 mg), the patient's trachea was extubated to nasal cannula, and he was admitted to the cardiothoracic intensive care unit (CTICU). We continued his nocturnal BiPAP 14/8. He denied postoperative pain and was comfortable without the administration of supplemental analgesic agents.

Follow-up and outcomes

On postoperative day 2, oral aspirin and warfarin were restarted. Subcutaneous heparin was continued until the international normalized ratio (INR) returned to 2 - 3. He was discharged home on postoperative day 4 and the remainder of his postoperative course was unremarkable.

Discussion

The need for non-cardiac surgery in patients supported with an LVAD has become more widespread because of increasing implantation of assist devices, their more prolonged use, and the long-term success of such devices leading to favorable and prolonged survival rates. Although general anesthesia is frequently chosen for such procedures, given increasing expertise with regional anesthesia including peripheral blockade with the use of ultrasound and improved anticoagulation management, it may be feasible to perform these procedures under regional anesthesia alone or as a combined general-regional technique as was done in our patient.

Regardless of the anesthetic technique, several factors

must be considered when providing anesthetic care for a patient with an implanted LVAD including the factors that control function of the LVAD and hence cardiac output, management of chronic anticoagulation therapy, the surgical procedure itself, and the associated comorbid conditions of the patient. The latter factor may or may not be related to the factors resulting in chronic myocardial dysfunction and the need for the LVAD. In our patient, this included his associated DMD, which aside from the need for the LVAD had significant impact on the perioperative care of our patient (see below). As with all anesthetic care, the first step includes a thorough preoperative history and physical examination to identify comorbid involvement related to the primary disease process and ensure that preoperative optimization of physiology function has been achieved. When considering the impact of LVAD on anesthetic care, the following factors determine blood flow through the device: the pressure gradient across the pump, the pump speed, and filling of the left ventricle (preload). An increased pressure gradient across the pump, caused by an increased in systemic vascular resistance (SVR), decreases flow (cardiac output) [5, 6]. This results in an inverse relationship between mean arterial pressure (MAP) and pump flow rate. Unlike the usual state, where changes in SVR may be compensated for by a change in cardiac output, this does not occur with an LVAD. Hence, as noted in our patient, with the induction of anesthesia and a decrease in SVR, the blood pressure (BP) decreases in a linear fashion. In our patient, the decrease in SVR related to the induction of anesthesia and the institution of positive pressure ventilation was treated by the administration of a direct acting α agonist, phenylephrine.

Another factor influencing perioperative care is management of anticoagulation therapy, not only for the surgical procedure, but also for placement of regional blockade. Bleeding complications after peripheral nerve blockade in patients treated with an antiplatelet agent and/or an anticoagulant medication are uncommon, with an estimated incidence of 0.67% (0.51-0.83%). Superficial lower extremity blockade of nerves that are close to large vessels (femoral nerve, femoral triangle, adductor canal, popliteal sciatic nerve) are considered as intermediate risk, whereas superficial blockade that is not in proximity to major vascular (lateral femoral cutaneous nerve, infrainguinal fascia iliaca, and ankle block) are classified as low risk for bleeding complications. Given the lower risk of bleeding complications, superficial nerve blockade may be performed in the presence of antithrombotic medications, irrespective of the dose. No routine testing of laboratory values is suggested for these procedures. Following superficial nerve procedures, the next dose may be administered at the routinely prescribed next time point.

Implantation of an LVAD and ongoing LV support requires systemic anticoagulation, which is frequently provided by oral warfarin therapy with a goal INR of 2 - 3, as well as the administration of an agent that inhibits platelet function (aspirin in our patient). The care plan for our patient included discontinuation of warfarin and aspirin 72 h prior to the procedure to allow the INR to slow return to the normal range. Subcutaneous low-molecular-weight heparin (LMWH) was started to provide anticoagulation with the ability to allow its effect to dissipate more rapidly by holding a dose prior to the planned surgical procedure. The literature does not provide specific recommendations for perioperative management of anticoagulation in LVAD patients. There is a relative absence of evidence-based medicine regarding this process with the literature containing retrospective reports of institutional experience, case series, or single case reports. Barbara et al [7] reported their retrospective experience with the perioperative management and outcomes of 67 non-cardiac surgical procedures in 33 patients support with an LVAD. In their series, the HeartMate II was the most commonly implanted LVAD, being used in 62 patients or 93% of their cohort. The most common indication was to treat LV dysfunction related to ischemic cardiomyopathy (25 patients or 37%). The most common anticoagulation/antiplatelet agents used for the patients were aspirin and warfarin (47%). Bridging anticoagulation (warfarin therapy withheld and anticoagulation continued with LMWH) was only reported in one patient (3%). The most common procedure was abdominal exploration (14 patients or 21%). No perioperative thrombotic complications related to anticoagulation or antiplatelet reversal were noted. Postoperative complications during hospitalization were present after 18 operations (27%), with 14 being bleeding related [6, 7].

Despite the increased need for surgical intervention during patient care with an LVAD, there are only three previous reports of regional anesthesia in these patients (Table 1) [8-10]. The literature includes a total of five adult patients, in whom regional anesthesia was the primary technique for a surgical intervention during use of an indwelling ventricular assist device (VAD). The age of the patients ranged from 24 to 72 years. Surgical procedures included Cesarean delivery, total knee replacement, and surgical debridement of infectious complications around the LVAD insertion site. Regional anesthetic technique included neuraxial technique (epidural) in one patient, a combined spinal anesthesia and adductor canal block in one patient, and regional blockade (thoracic paravertebral) in three patients.

We present our experience with the use of regional blockade combined with deep sedation/general anesthesia for intraoperative anesthesia in a patient with DMD and an indwelling LVAD. Given the concerns regarding the impact of changes in preload and afterload on hemodynamic function, anesthesia was induced with midazolam and etomidate [11]. Given the associated DMD, TIVA was chosen due to concerns of hyperkalemia with prolonged administration of volatile anesthetic agents. TIVA included a combination of dexmedetomidine and remimazolam. The latter was added to ensure amnesia and allow for rapid awakening and limited impact on postoperative respiratory function [12, 13]. Given the presence of chronic respiratory insufficiency with BiPAP dependence, we chose to use short-acting agents with limited impact on respiratory drive for intraoperative anesthesia (dexmedetomidine and remimazolam) and avoidance of high doses of opioids by using regional anesthesia for surgical and postoperative analgesia. The only intraoperative opioid administered was hydromorphone (1 mg), administered at the time of anesthetic induction. As the fractures were at the distal femur and proximal tibia, blockade of both the femoral and popliteal nerves were required.

Table 1. Reports Regarding Regional Anesthesia for LVAD Patients Undergoing Surgical Interventions

Author	Age/sex	Surgical procedure	Anesthesia type/comments
Gayam et al, 2020 [8]	24-year-old woman, 80 kg with LVAD (polysubstance abuse-related cardiomyopathy)	Induction of labor and Cesarean delivery	Epidural anesthesia. The last dose of enoxaparin (150 mg twice daily) was 24 h before admission. The epidural was incrementally dosed with 15 mL of 0.125% bupivacaine and 5 mL of 0.25% bupivacaine over a 1.5-h period of time. Analgesia was then maintained with an infusion of 0.1% bupivacaine and fentanyl 2 µg/mL. Cesarean delivery proceeded uneventfully. Anticoagulation was resumed on POD 1 using an unfractionated heparin infusion at 700 U/h and then transitioned to dabigatran. Bilateral transverse abdominis plane blocks using liposomal bupivacaine were performed on POD 1 and 6.
Fegley et al, 2021 [9]	72-year-old woman with LVAD for ischemic cardiomyopathy	Elective left TKR	Spinal anesthesia (L3 - 4) and adductor canal catheter. Sedation was provided using a propofol infusion. Warfarin was withheld 6 days before surgery and the patient was admitted to the hospital 2 days before surgery for maintenance of anticoagulation with intravenous unfractionated heparin. The heparin infusion was discontinued 4 - 6 h before the procedure. Anticoagulation was reinitiated on POD 2, after removal of the adductor canal catheter. The patient's postoperative course was uncomplicated. She was discharged home on POD 5.
Okitsu et al, 2017 [10]	Case series of three patients (35 - 49 years of age). One male and two females with an LVAD for dilated cardiomyopathy	Surgical management of LVAD-related infections	Combined general and regional anesthesia (continuous TPVB). Warfarin therapy was not altered for catheter placement or removal. Levobupivacaine (10 mL of 0.25%) was administered during catheter insertion for the intraoperative analgesic and 0.125% levobupivacaine was continuously infused at a rate of 6 mL/h postoperatively for 3 days to 2 weeks. Satisfaction ranged from 5 - 8/10.

POD: postoperative day; LVAD: left ventricular assisted device; TKR: total knee replacement; TPVB: thoracic paravertebral block.

Learning points

DMD is an X-linked recessive genetic disorder related to mutations in the dystrophin gene. Although dysfunction of the dystrophin complex leads initially to skeletal muscle involvement, progressive effects on myocardial function and the eventual development of cardiomyopathy generally become clinically evident during the teenage years or early adult life. Cardiac failure is the most common cause of death in the second and third decade of life. With advancements in technology and anticoagulation therapy, long-term outpatient support with VADs is now feasible. This has resulted in a growing population of patients with indwelling LVADs who may require surgical intervention. In these patients, perioperative concerns include DMD and its associated end-organ effects, rhabdomyolysis and hyperkalemia from prolonged exposure to volatile anesthetic agents, management of chronic anticoagulation, hyperthermia, and the impact of anesthetic agents on preload/afterload and hemodynamic function with an indwelling LVAD. Regional anesthetic techniques may be used successfully in patients with muscle dystrophies as an adjunct to or instead of general anesthesia to provide a stable intraoperative course.

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None to declare.

Financial Disclosure

None to declare.

Conflict of Interest

None to declare.

Informed Consent

Written consent was obtained for anesthetic care and use of deidentified information for publication.

Author Contributions

AE contributed to case review and preparation of manuscript. GH, MAV, and MC provided clinical care, manuscript review, and editing. JDT contributed to manuscript preparation, review, and editing.

Data Availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

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