Clinical Reports

Neuromuscular relaxants in non-cardiac surgery after cardiomyoplasty

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Purpose: Dynamic cardiomyoplasty is a therapeutic alternative to heart transplantation in irreversible cardiac insufficiency. Little information exists about the use of muscle relaxants in patients with cardiomyoplasty. In particular, it is not clear if the muscle flap is responsive to neuromuscular blockers. The purpose of this report is to describe the safe use of vecuronium in a patient with cardiomyoplasty.

Clinical features: A 59-yr-old man, after cardiomyoplasty for dilated cardiomyopathy two years earlier, underwent general anaesthesia with fentanyl, propofol and vecuronium during surgery for intestinal ischaemia. Intraoperative transthoracic echocardiography showed that vecuronium did not affect muscle flap motion. Two days after surgery he died in septic shock. Post-mortem histological and immunohistochemical examination showed nervous degeneration of the flap probably as a result of the chronic low frequency pacing. There was also an increase in extrajunctional receptors and an alteration in junctional receptors, as demonstrated by the negative reaction to anti-synaptophysin antibodies, used to identify the neuromuscular plate.

Conclusion: In patients undergoing non-cardiac surgery after previous cardiomyoplasty, muscle relaxants, such as vecuronium, may be used safely. Depolarising agents, such as succinylcholine, should probably be avoided because of the possible exaggerated actions on extrajunctional receptors.

Objectif : La cardiomyoplastie dynamique est une alternative thérapeutique à la greffe cardiaque dans l'insuffisance cardiaque irréversible. Il existe peu d'information sur l'utilisation des relaxants musculaires chez les patients ayant subi une cardiomyoplastie. De façon plus précise, la réponse du lambeau musculaire aux bloqueurs neuromusculaires est controversée. Le but de cet article est de décrire l'utilisation sécuritaire du vécuronium chez un patient ayant subi une cardiomyoplastie.

Aspects cliniques : Un homme de 59 ans, ayant subi une cardiomyoplastie il y a 2 ans pour une cardiomyopathie, a subi une anesthésie générale à base de fentanyl, propofol et vécuronium pour une chirurgie pour ischémie intestinale. Une échographie transthoracique peropératoire a démontré que le vécuronium ne modifiait pas le mouvement du lambeau musculaire. Deux jours après son opération il est décédé de choc septique. L'examen post-mortem tant histologique qu'immunohistochimique a montré une dégénérescence du tissu nerveux du lambeau, probablement comme conséquence de la stimulation chronique à basse fréquence. On retrouvait aussi une augmentation des récepteurs membranaires extrajonctionnels et une altération des récepteurs jonctionnels, tel que démontré par la réaction négative aux anticorps antisynaptophysine, utilisés pour identifier les jonctions neuromusculaires.

Conclusion : Chez les patients subissant une chirurgie non cardiaque après cardiomyoplastie, les relaxants musculaires, tel le vécuronium, peuvent être utilisés sécuritairement. Les agents dépolarisants, tel la succinylcholine, devraient probablement être évités à cause des risques d'effets excessifs sur les récepteurs extrajonctionnels.

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Accepted for publication January 11, 1998.

DYNAMIC cardiomyoplasty is a therapeutic alternative to heart transplantation in irreversible cardiac insufficiency. With this operation, the *latissimus dorsi* muscle is mobilised, drawn into the thorax and sutured around the heart with its neurovascular bundle intact. The skeletal muscle is stimulated by an implanted cardiomyostimulator, which is programmed to fire synchronously with ventricular systole.[1,2] After 6–8 wk of muscular conditioning, the flap is transformed into a slow-twitch, fatigue-resistant muscle. Pacing is accomplished by stimulation of the muscle directly, and indirectly via the intact nerve fibres to the *latissimus dorsi*, so that the muscle will contract in an all or none manner.[3] According to Chachques and colleagues dynamic cardiomyoplasty appears to exert its beneficial effects by improving ventricular contraction and by limiting cardiac dilation.

More information is needed about the feasibility of general anaesthesia in non-cardiac surgery after cardiomyoplasty, and little is known about the response of the muscular flap to neuromuscular blockers, except for few speculative reports.[3,4]

Case report

A 59-yr-old, 65-kg man, who had undergone cardiomyoplasty for dilated cardiomyopathy two years earlier (in another istitution), was admitted with end-stage cardiac failure (dyspnea, hypotension, ejection fraction of 10%) and ventricular arrhythmias, as premature ventricular contractions and runs of slow ventricular tachycardia, for heart transplant. Intravenous therapy (dobutamine, furosemide, lidocaine) partially controlled the symptoms but the patient was still NYHA class IV. Two-dimensional echocardiography showed marked left ventricular dilation (71 mm), paradoxical septal motion, severely depressed left ventricular function, and a functioning flap. There was mild-to-moderate mitral insufficiency and mild aortic regurgitation, with early systolic closure of the cusps. The left atrium was dilated, the tricuspid valve was moderately incompetent and the Doppler-estimated pulmonary artery pressure was 45 mmHg. The right atrium, inferior vena cava and supra-hepatic veins were markedly dilated. There was no pericardial effusion. During hospitalisation, the patient suffered acute intestinal volvulus requiring emergency surgery. The operation was performed (in a non-cardiac surgery theatre) using epidural anaesthesia. The postoperative period was complicated by acute respiratory failure and severe hypotension, requiring tracheal intubation and norepinephrine infusion (0.08 $\mu g \cdot kg^{-1} \cdot min^{-1}$). Two days later the patient developed intestinal ischaemia that required urgent surgery (in cardiac surgery theatre) under general anaesthesia. The trachea was already intubated and the lungs were being ventilated with O_2/air (FiO_2 = 45%) to maintain $PaCO_2$ < 40 mmHg. Laboratory investigations showed haemoglobin = 12.1 $g \cdot dL^{-1}$, BUN 18.4 $mMol \cdot L^{-1}$, creatinine 132 $mMol \cdot L^{-1}$ and metabolic acidosis (HCO_3^- 17.1 $mEq \cdot L^{-1}$). General anaesthesia was induced with 7 $\mu g \cdot kg^{-1}$ fentanyl and 1 $mg \cdot kg^{-1}$ propofol given over 60 sec, maintaining the same ventilatory settings. Monitoring included five-lead ECG, invasive blood pressure (BP), central venous pressure (CVP), pulse oximetry and end-tidal capnography (Table). Intraoperative transthoracic echocardiographic monitoring was performed using a 3.25 MHZ probe to control cardiac function and performance of the muscular flap during vecuronium administration (Table). Vecuronium was

TABLE Haemodynamic and echocardiographic parameters during vecuronium administration.

	Baseline	*Induction*	*Vecuronium administration*					
			1 mg	*2 mg*	*3 mg*	*4 mg*	*5 mg*	*6 mg*
HR (bpm)	112	118	115	113	108	104	105	106
SAP (mmHg)	82	75	78	80	82	85	90	95
MAP (mmHg)	61	60	62	60	65	66	65	66
DAP (mmHg)	55	48	53	54	55	55	56	55
CVP (mmHg)	18	17	17	15	14	15	15	16
SpO_2 (%)	97	96	98	98	98	99	99	99
$P_{ET}CO_2$ (mmHg)	34	36	34	34	32	32	30	30
LVEDD (mm)	55	55	54	54	53	52	52	51
LVESD (mm)	52	51	51	51	49	48	48	48
LVEDV (ml)	216	214	211	209	205	201	198	198
LVESV (ml)	190	189	185	183	175	170	167	165
EF (%)	12	12	12	13	15	15	16	17

HR = heart rate; SAP = systolic arterial pressure; MAP = mean arterial pressure; DAP = diastolic arterial pressure; CVP = central venous pressure; SpO_2= oxygen saturation; $P_{ET}CO_2$ = end-tidal CO_2; LVEDD = left ventricular end- diastolic diameter; LVESD = left ventricular end-systolic diameter; LVEDV = left ventricular end-diastolic volume; LVESV = left ventricular end-systolic volume; EF = ejection fraction.

given in incremental doses of 1 mg every 1.5 min up to a total dose of 6 mg to achieve complete muscular paralysis of the adductor pollicis (Digisistem 3 plus Organon Teknika - Belgium). At baseline, BP was 82/55 mmHg, CVP 18 mmHg and heart rate (HR) 112 bpm; after induction but before vecuronium administration, BP was 75/48 mmHg, CVP 17 mmHg and HR 118 bpm. During vecuronium administration there was a progressive improvement in lateral wall motion leading to a reduction in left ventricular volumes and increase in ejection fraction (Table). The degree of valvular regurgitation remained unchanged. The BP increased to 95/55 mmHg, while the HR was reduced by 10% (Table). Anaesthesia was maintained with propofol and fentanyl infused at a rate of 6 $mg \cdot kg^{-1} \cdot hr^{-1}$ and 10 $\mu g \cdot kg^{-1} \cdot hr^{-1}$, respectively. Supplementary vecuronium (0.04 $mg \cdot kg^{-1}$) was administered according to neuromuscular monitoring. Fluid balance during the operation was +300 ml; 350 ml of blood were lost and the patient was not transfused. Two days later the patient died of septic shock.

At postmortem examination, the heart was enlarged and the obtuse margin was covered by a thin layer of latissimus dorsi muscle, with no gross lesions. On the cut surface, all cardiac cavities were dilated and there were neither myocardial scars, nor valvular abnormalities. The coronary tree was unremarkable, except for intramyocardial tunnelling of the proximal tract of the left anterior descending artery. Histology showed features of idiopathic dilated cardiomyopathy. The muscle flap revealed neurogenic atrophy characterised by spotty myocyte atrophy intermingled with hypertrophic and normal areas. Several fibres displayed an irregular shape and centralisation of nuclei. Fibro-fatty substitution was extensive. The S 100 immunohistochemical staining was used to identify nerve fibres, which appeared to be only slightly less represented than in control muscle. Anti-synaptophysin antibodies, used to identify the neuromuscular plate, failed to stain.

Discussion

Dynamic cardiomyoplasty presents some advantages over cardiac transplantation because it is not dependent on the availability of donor organs, and it does not require either cardiopulmonary bypass or immunosuppression. About five hundred patients in the world have received cardiomyoplasty as temporary or definitive treatment of end-stage cardiac failure. This large number represents a considerable challenge for the anaesthetist when further surgery with general anaesthesia is needed.[3,5] Little information exists about the safe use of muscle relaxants in patients with cardiomyoplasty.[3,4] In particular, it is not clear why the muscle flap is not responsive to neuromuscular blockers.[6] To our knowledge, only two patients with cardiomyoplasty have undergone general anaesthesia that included the use of atracurium, one for replacement of a cardiomyostimulator and the other for inguinal herniorrhaphy.[3] Greenhalgh *et al.*[4] discourage the use of depolarising agents, while others speculate that non-depolarising agents can be safely employed, because the grafted muscular tissue is extensively replaced by fibrous tissue.[3]

In our patient, fibro-fatty substitution was intermingled with hypertrophic and normal muscular fibres. Furthermore, despite the evidence of neurogenic atrophy, there were intact nerve fibres, only slightly less represented than in control muscle. Pacing of the cardiomyoplasty flap is accomplished by stimulation of the muscle directly and indirectly, via the intact nerve fibres to the latissimus dorsi, so that the muscle will contract in an all-or-none manner.[3] Therefore, the absence of neuromuscular junctions at autopsy, may not be evidence of the flap not working. In addition, intraoperative echocardiography showed a functioning flap. The muscular flap underwent nervous degeneration because of chronic low frequency pacing.[7] This may promote an increase in extrajunctional and an alteration in junctional receptors,[8,9] as demonstrated by the negative reaction to anti-synaptophysin antibodies, used to identify the neuromuscular plate. Extrajunctional receptors may be resistant to non-depolarising relaxants at doses required to produce clinical neuromuscular block.[9] In fact, to block transmission at extrajunctional receptors greater doses of non-depolarising muscle relaxants are necessary.[9] We have observed that vecuronium administration had a positive impact on left ventricular function. It caused a reduction in HR and an improvement in left ventricular function. According to Greenhalgh *et al.*,[4] we think that the use of depolarising muscle relaxants, which induce fasciculation, hyperkalaemia and could compromise cardiac output, should be avoided considering also their action on extrajunctional receptors.

In conclusion, in cardiomyoplasty patients undergoing non-cardiac surgery, muscle relaxant agents should be chosen considering the complex effects of these drugs on junctional and extrajunctional receptors. In particular, succinylcholine should probably be avoided because of its action at extrajunctional receptors.[9] Vecuronium, like other non-depolarising agents, can be safely employed because of resistance of the extrajunctional receptors that are present in the muscular flap.

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