Letters to Editor

Anaesthesia for non-cardiac surgery in a cardiac transplant recipient

Sir,

We read with interest the article of Swami *et al*.[1] concerning anaesthesia for non-cardiac surgery in a heart-transplanted patient. I congratulate them on the careful presentation of the case. Likewise, I would like to address the issue of the lack of effect of anticholinesterases and vagolytic drugs on heart rate (HR). The authors assert that "the transplanted heart has no sympathetic, parasympathetic or sensory innervation", and later claim that "In the transplanted heart, the HR shows no response to drugs like… anticholinergics (atropine…) and anticholinesterases (neostigmine, edrophonium…)". I should say it is risky to make these claims.

The surgical procedure of heart transplantation preserves the donor sinus node function, although in an autonomically denervated state. In a minority of cases with biatrial anastomosis, the native sinoatrial (SA) node may also still be present and continue to function, although the discharge is not conducted across the suture line. The donor heart relies on the denervated function of the donor SA node for its pacemaker.[2] It was thought that interrupted autonomic input was permanent. However, consistent evidence indicate that, with time, some degree of sympathetic and parasympathetic reinnervation is reestablished,[2,3] progressively, but is likely not complete until 15 years after transplantation.[4] Thus, efferent sympathetic fibers are present in 80% of transplant patients 3 years after transplantation. This explains the frequent complaint of angina and improved HR and contractile response to exercise in heart recipients.[4] Likewise, the presence of HR variability with respiration or changes in posture and vasovagal syncopal episodes in some heart-transplanted patients suggest parasympathetic reinnervation.[5] It is necessary to consider the physiologic repercussion when reinnervation occurs.

Neostigmine causes bradycardia by its anticholinesterase action, preventing the hydrolysis of acetylcholine (ACh) tonically released by neurons in the cardiac parasympathetic pathway. Accordingly, it was thought that neostigmine would have no effect on HR in denervated heart-transplant patients because, presumably, there was little or no evoked release of Ach from parasympathetic neurons. However, neostigmine has been shown to produce an atropine-sensitive dose-dependent bradycardia in both recently and remotely transplanted patients,[5] the probability of response increasing with the post-transplant time span. Some remotely transplanted patients are particularly sensitive, demonstrating greater bradycardia responses.[2] In addition, asystole preceded by bradycardia and sinus arrest after administration of neostigmine for reversal of neuromuscular blockade has been reported in several heart transplant patients.[2,3,6,7] Edrophonium also produces bradycardia in cardiac transplant recipients, although the decrease in HR is smaller in magnitude and much more consistent compared with neostigmine. In addition, HR increase in response to atropine is similar and slower than in native hearts.[6] The mechanism by which this occurs appears to be variable parasympathetic reinnervation and/or direct stimulation of nicotinic cholinergic receptors on the post-ganglionic parasympathetic neurons with release of ACh from their terminals and subsequent activation of inhibitory cardiac receptors.[5] Moreover, there is allograft denervation hypersensitivity of both the post-ganglionic neurons and the muscarinic myocardial receptors to the cholinergic agonist effect of neostigmine.[3] These factors, combined with intrinsic allograft SA node dysfunction, may produce severe dysfunction or sinus arrest after acetylcholinesterase inhibitor administration in heart transplant patients.

Caution should be exercised when reversing neuromuscular block with the anticholinesterase even when a muscarinic antagonist is coadministered. Reduction in HR should be anticipated. Avoidance of neuromuscular block if possible, use of short-acting drugs if paralysis is required or use of new reversal agents such as sugammadex are strategies to avoid a potentially catastrophic response to neostigmine.[3,6] If anticholinesterase drugs are used, a muscarinic antagonist should always be co-administered and potent β-adrenergic agonists such as isoproterenol or epinephrine should be readily available.

Manuel Á Gómez-Ríos

Department of Anaesthesiology and Perioperative Medicine, University Hospital Complex of A Coruña, Galicia, Spain

Address for correspondence:
Dr. Manuel Á Gómez-Ríos,
Department of Anaesthesiology and Perioperative Medicine,
University Hospital Complex of A Coruña, Galicia, Spain.
E-mail: magoris@hotmail.com

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