Rev Bras Anestesiol. 2014;64(1):40–48

REVISTA BRASILEIRA DE ANESTESIOLOGIA

Official Publication of the Brazilian Society of Anesthesiology
www.sba.com.br

SCIENTIFIC ARTICLE

Intravenous clonidine administration and its ability to reduce pulmonary arterial pressure in patients undergoing heart surgery

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Received 21 October 2012; accepted 20 March 2013

KEYWORDS
Clonidine;
Pulmonary hypertension;
Heart surgery

Abstract
Objective: Evaluate the ability of clonidine to reduce pulmonary arterial pressure in patients with pulmonary hypertension undergoing heart surgery, either by reducing the pressure values from the direct measurement of pulmonary arterial pressure or by reducing or eliminating the need for intraoperative dobutamine and nitroprusside.
Method: Randomized, double-blind, placebo-controlled, comparative study conducted in 30 patients with pulmonary arterial hypertension type 2 undergoing cardiac surgery. Mean pulmonary arterial pressure and dosage of dobutamine and sodium nitroprusside were assessed four times: before intravenous administration of clonidine (2 μg/kg) or placebo (T0), 30 min after tested treatment and before cardiopulmonary bypass (T1), immediately after CPB (T2), 10 min after protamine injection (T3).
Results: There were no significant differences regarding mean pulmonary arterial pressure at any time of evaluation. There was no significant difference between groups regarding other variables, such as mean systemic arterial pressure, heart rate, total dose of dobutamine, total dose of sodium nitroprusside, and need for fentanyl.
Conclusion: Data analysis from patients included in this study allows us to conclude that intravenous clonidine (2 μg/kg) was not able to reduce the mean pulmonary arterial pressure in patients with pulmonary hypertension in group 2 (pulmonary venous hypertension), undergoing heart surgery, or reduce or eliminate the need for intraoperative administration of dobutamine and sodium nitroprusside.

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0104-0014
http://dx.doi.org/10.1016/j.bjane.2013.03.019

Introduction

Pulmonary hypertension (PH) is a chronic disease defined by high mean pulmonary arterial pressure above 25 mmHg at rest or 30 mmHg on exertion. Due to its varied etiology, PH is associated with three major deleterious phenomena: vascular remodeling, hypoxic vasoconstriction, and in situ thrombosis. PH is difficult to control and evolves with hypoxemia, increased resistance to ejection of blood by the right ventricle (RV), RV failure, and death.[1]

PH is classified into five groups: (I) pulmonary arterial hypertension (includes the idiopathic form); (II) pulmonary hypertension associated with left heart diseases; (III) pulmonary hypertension associated with respiratory disease and/or hypoxemia; (IV) pulmonary hypertension due to chronic thrombotic and/or embolic disease; and (V) miscellaneous group.[1]

PH is most often found in group II patients, as a result of left ventricle (LV) failure associated with other common heart disease progression, such as valvular heart disease and coronary artery disease.[2] Myocardial failure makes the LV unable to eject blood into the systemic circulation that reaches the left heart through the pulmonary veins. The high pressure of the pulmonary venous bed is transmitted backward to the arterial system. For no other reason, PH of group II is referred to as pulmonary venous hypertension (PVH).[3]

Anesthesia in these patients is an enormous challenge because it is necessary to control both the ventricular disease and pulmonary hypertension. To face it, various combinations of drugs are used, including the association of inotropic dobutamine (DBT) and the vasodilator sodium nitroprusside (NTP), which is one of the more frequently used. However, to be effective, it is often necessary to use high doses of these agents. Undesirable effects may arise, such as tachycardia with the use of dobutamine or increased intracranial pressure, coronary steal, intrapulmonary shunt, and metabolic acidosis with sodium nitroprusside.[4] Thus, the pharmacological options available are not without side effects, which justify the interest for new therapeutic options.

Clonidine, a α_2-adrenergic, imidazole agonist, was introduced into clinical practice in the early 1960s. This drug was first proposed as a nasal decongestant, but soon its systemic effects became known, such as hypotension, bradycardia, and sedation.[5]

Due to the hypotensive effect of clonidine, which decreases the exocytosis of noradrenaline in the synaptic cleft, both in the central and peripheral nervous system,[6] it is now prescribed for hypertension management. In recent decades, this agent was studied as an adjunct to anesthesia. The advantages of clonidine in this context were recognized and its use spread also in the field of anesthesia in cardiac surgery. Among other benefits, clonidine is known to reduce the need for opioids intra- and postoperatively, which allows early tracheal extubation and shortens the duration of mechanical ventilation; hemodynamic stability at lower levels of circulating catecholamines; increased diuresis due to inhibition of the release of antidiuretic hormone (ADH); and release of atrial natriuretic factor.[6]

The presence of α_2-adrenergic receptors in lung tissues[7–9] and its central hypotensive action seem to indicate that clonidine may also be useful for treating PH patients undergoing heart surgery.

Methods

After approval by the Ethics Committee of the Hospital São Paulo (Unifesp) and Hospital Beneficência Portuguesa (São Paulo-SP) and obtaining signed informed consent from all participants, 30 patients of both sexes, physical status ASA II or III, aged between 18 and 80 years, with pulmonary hypertension secondary to left heart disease were enrolled in the study between January 2009 and December 2010. Due to the expiration date of the batch of drugs, one patient was excluded from the study.

Patients underwent cardiac surgery with cardiopulmonary bypass for valvular correction or myocardial revascularization.

The diagnosis of pulmonary hypertension was previously confirmed by right heart catheterization and defined by mean pulmonary arterial pressure greater than 25 mmHg at rest.

After fasting for 8 h, the patients were taken to the operating room without receiving pre-medication. In the operating room, they were monitored with electrocardioscope on DII and V5 derivations and, pulse oximetry, and for noninvasive blood pressure. All patients underwent venipuncture and intravenous administration of 3 mg midazolam. After this step, left or right radial artery was cannulated with a catheter caliber 20G for direct blood pressure measurement and blood sample collection for laboratory testing.

Anesthesia consisted of preoxygenation for 3 min, followed by administration of fentanyl (10 μg/kg), etomidate (0.4 mg/kg), pancuronium (0.1 mg/kg), lidocaine (1 mg/kg), facemask ventilation with 100% oxygen for 5–7 min, followed by intubation and maintenance with 1% isoflurane in oxygen and air (1:1). After tracheal intubation, monitoring was complemented by analysis of anesthetic gases, capnometry, and capnography.

Intraoperatively, we try to maintain mean arterial pressure between 50 and 80 mmHg with additional doses of fentanyl (5 μg/kg) and, if necessary, sodium nitroprusside. Cases of hypotension were treated according to the etiology, either with volume management or with inotropic, chronotropic or vasopressor agents.

After sternotomy and retractor placement, an 18G teflon catheter was placed under direct vision into the pulmonary artery to allow direct measurement of pulmonary artery pressure.

During cardiopulmonary bypass, in order to keep patients under hypnosis and immobility, midazolam (0.3 mg/kg) and pancuronium (0.1 mg/kg) were administered again. At the end of this stage, all patients were treated with dobutamine (5–10 μg/kg/min), in order to ensure hemodynamic stability (compensating for impaired myocardial contractility by ischemia-reperfusion and heart manipulation during cardiopulmonary bypass).

Categorical variables, such as age, weight, gender, and diagnosis were evaluated. Mean arterial pressure (MAP), heart rate (HR), mean pulmonary artery pressure (MPAP),