

REVIEW ARTICLE

Dexmedetomidine in pulmonary hypertension: A Review

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ABSTRACT

Patients with pulmonary hypertension often have adverse outcomes after anesthesia. Tachycardia, hypertension, hypervolemia, increased intrathoracic pressure, acidosis, painful stimuli and hyperthermia are triggering factors for adverse perioperative events.

Dexmedetomidine is a centrally acting α_2 agonist which, due to its desirable properties like sympatholysis, bradycardia and μ agonism, can be a useful agent for patients with pulmonary hypertension. Dexmedetomidine also has the ability to potentiate inhalational, intravenous and regional anesthetics when it is used as an adjunct.

Key words: Pulmonary arterial hypertension; Dexmedetomidine; Anesthesia.

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INTRODUCTION

Pulmonary artery hypertension (PAH) is a condition in which patients can have significant cardiorespiratory issues when exposed to any anesthetic technique for any surgical or diagnostic intervention. They have to be adequately investigated and optimized before any active intervention. Anesthesia management of a patient with PAH is very challenging task. Pulmonary hypertension is classified as PAH (idiopathic, familial, due to congenital heart disease, infections, drugs and / or toxins etc), due to left heart disease, secondary to lung disease or chronic hypoxemia, due to thromboembolic disease and miscellaneous causes due to lymphangiomatosis secondary to carcinoma, sarcoidosis, pulmonary vascular compression.¹ PAH is defined as mean pulmonary artery pressure above 25 mmHg at rest and above 30 mmHg during exercise in a normal or reduced cardiac output or normal pulmonary capillary pressure. Knowledge of pathophysiology of PAH, implications of anesthetic technique or anesthesia agent on pulmonary vascular resistance (PVR) is very important.² Detailed history, multidisciplinary optimization, meticulous monitoring with identification and management of catastrophic events is essential for the successful management of a patient with PAH.

IMPLICATIONS OF ANESTHESIA IN PAH

Surgical or procedural intervention of any kind under

any anesthetic technique can lead to significant morbidity and mortality in patients with severe pulmonary artery hypertension (PAH) irrespective of the cause of PAH. The reason of morbidity or mortality could be right ventricular failure, life threatening arrhythmias, myocardial infarction, post operative hypoxemia leading to ventilator support and prolonged ICU stay. Ramakrishna et al reviewed 145 patients with pulmonary hypertension over a period of 12 years who underwent non cardiac surgeries and found that morbidity and mortality was around 7%.³ Friesen et al in their review article discussed in great detail the pathophysiology of pulmonary hypertension, the importance of judicious and balanced anesthesia technique and management of pulmonary hypertensive crisis in children with pulmonary hypertension.⁴ Kozarek et al and Shukla et al in their review article described the pathophysiology and classification of pulmonary hypertension and also discussed the intraoperative and postoperative management of these patients coming for surgery.^{5,6} Meticulous preoperative evaluation, judicious intraoperative management, prompt diagnosis and management of adverse events are key points in the management of patients with PAH. Pritts and Pearl in their review article suggested that the cause of PAH should be investigated and preoperative optimization is necessary.⁷ One of the most elaborate and detailed review article was published by Fischer et al almost a decade ago in which they described pulmonary circulation,

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pathophysiology of pulmonary hypertension, causes of PAH, symptomatology of PAH, modalities of diagnosis and treatment of pulmonary hypertension.⁸ The review also described effects of routinely used anesthetic drugs on pulmonary vascular tone and right heart function in humans.

Intraoperative factors like hypoxemia, hypercarbia, acidosis (respiratory or metabolic), pain, increased intrathoracic pressure, hypothermia, hypervolemia and intubation or extubation response can exacerbate existing problems leading to morbidity. Any perioperative factor which increases pulmonary vascular resistance (PVR) can lead to a serious event. All the above mentioned factors can lead to increase in PVR leading to major adverse cardiac events. Precipitous hypotension (by using intravenous induction agents like thiopental, propofol) should be avoided. Intermittent positive pressure ventilation (IPPV) can also affect the right ventricular preload and can deleterious effects. Salehi A has highlighted how the choice of anesthesia technique and the effects of anesthesia drugs affects the pulmonary vascular resistance.⁹ Hence euvolemia is very important. The aim should be to maintain sinus rhythm. Electrolyte imbalances should be rectified prior to induction. Subramaniam K et al described the strategies of management of a patient with PAH specifically in the operating room.¹⁰ Ideally fluid management in major surgeries should be guided by floating a pulmonary artery catheter and monitoring wedge pressure. But pulmonary artery catheterization is controversial and difficult in presence of severe PAH. Hence it should be used by personnel who are fairly experienced with the procedure and when the situation demands it like in surgeries involving major blood loss and extensive fluid shifts. Use of central venous catheter is recommended by many, for anticipated use of cardiac medications like inodilators, prostacyclin analogues etc. But these procedures can lead to arrhythmias which can have catastrophic outcomes in patients with severe PAH as the right atrial and ventricular wall is thinned out can be proarrhythmic. Gille et al have mentioned that in patients who are class I/II, basic monitoring like pulse oximetry, ECG, end tidal carbon dioxide and an invasive arterial blood pressure monitoring is enough.¹¹ Advanced monitoring e.g. wedge pressure, PA pressure, TEE, mixed venous saturation and stroke volume variation, is mandatory for functional class III and beyond.

DEXMEDETOMIDINE IN PAH

Dexmedetomidine is a centrally acting α_2 agonist approved for procedural sedation and for sedation in intensive care units for less than 24 hrs. It exerts its action when administered intravenously at several sites like brain, spinal cord and peripheral vasculature. Initially, a loading dose of

1 $\mu\text{g}/\text{kg}$ has to be administered intravenously over 10-15 minutes followed by an infusion @ 0.2-0.7 $\mu\text{g}/\text{kg}/\text{hr}$. In brain, dexmedetomidine exerts its effects by acting on locus ceruleus and leads to sedation which mimics natural sleep. It causes sympatholysis by acting on α_2 receptors in locus ceruleus, reduces the heart rate and causes sympatholysis induced vasodilatation, due to which there can be hypotension in hypovolemic patients.^{12,13} This sympatholysis attenuates hemodynamic response to intubation and extubation. Dexmedetomidine potentiates the effects of intravenous, inhalational anesthetics and regional anesthesia as well. The requirement of narcotics is also reduced.^{14,15} By causing sympatholysis, dexmedetomidine attenuates the hypertensive hemodynamic response to extubation / intubation and also provides a low heart rate. By acting at spinal cord and potentiating analgesic effects of narcotics; dexmedetomidine has an opioid sparing effect, requirement of inhalational anesthetic agents is reduced and the emergence is smooth without any hemodynamic response.¹⁶ Owing to these properties of dexmedetomidine, it can be an adjunct in the anesthesia management of a patient with pulmonary hypertension with general and regional anesthesia and as the sole anesthetic for procedural sedation for diagnostic and minimally invasive procedures. Other important factors like oxygenation, hypercarbia, intravascular volume, hemodynamics etc should be addressed and optimized effectively. Nathan et al described the use of dexmedetomidine in a 16 year old patient with significant pulmonary hypertension in whom they used the drug for procedural sedation without intubation uneventfully. They successfully discharged the patient from the hospital.¹⁷ Munro et al used 1 mg/kg ketamine and 1 $\mu\text{g}/\text{kg}$ of dexmedetomidine loading dose followed by 1 $\mu\text{g}/\text{kg}$ of dexmedetomidine in a 12 years old boy with idiopathic PH for cardiac catheterization study successfully.¹⁸ They continued the infusion for 2 hrs after the procedure for smooth emergence. Toyoma et al used IV dexmedetomidine in a 30 yr old, 32 weeks parturient with primary pulmonary hypertension, who underwent cesarean section under general anesthesia. Agents like nitric oxide, dobutamine, nitroglycerin and prostacyclin was also used perioperatively. Dexmedetomidine helped in hemodynamic stability and smooth emergence from anesthesia.¹⁹ Shinohara et al used dexmedetomidine in a young male for hernioplasty who was diagnosed with severe PH owing to congenital heart disease and was having dyspnea of functional class IV. He was given ultrasound guided ilioinguinal and iliohypogastric nerve blocks and was started on dexmedetomidine infusion. There were no hemodynamic issues during this surgery.²⁰

Anesthesiologist should be very careful while using dexmedetomidine in patients with severe biventricular dysfunction, in renal and hepatic impairment. Dose adjustment is required in patients with renal and hepatic

impairment and in elderly patients where sinus arrest has been reported with dexmedetomidine in patients with sinus bradycardia. This can be avoided by premedicating these patients with either atropine or glycopyrrolate. While using general anesthesia, a balanced anesthetic technique with judicious use of narcotics, inhalational anesthetics, benzodiazepines and intravenous anesthetic agents should be done to avoid hemodynamic compromise, to provide good anesthetic depth, provide good analgesia and an uneventful outcome.

Patients with pulmonary hypertension are usually on cardiac medications like phosphodiesterase V inhibitors (sildenafil, tadalafil etc), endothelin antagonists (Bosentan), diuretics (furosemide, spironolactone), calcium channel blockers, angiotensin converting enzyme (ACE) inhibitors which should be administered preoperatively and continued perioperatively. Centers having the facility of inhaled nitric

oxide can use it in case there is a pulmonary hypertensive crisis due to worsening of PVR. Drugs like milrinone, noradrenaline, dobutamine, prostacyclin analogues (Epoprostenol) should be available and used whenever indicated.

CONCLUSION

Dexmedetomidine is a useful adjunct when used judiciously in patients with pulmonary artery hypertension by an experienced anesthesiologist. It can be used during general anesthesia, regional anesthesia or during procedural sedation in recommended doses with strict hemodynamic monitoring. In elderly patients and in patients with renal and hepatic dysfunction dose adjustment has to be done. It is relatively contraindicated in patients with sinus bradycardia, severe left ventricular dysfunction and hypovolemic states.

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