The Heart Surgery Forum 2022-5139
26 (1), 2023 [Epub January 2023]
doi: 10.1532/hsf.5139

Online address: http://journal.hsforum.com

Amlodipine and Atropine for Hypoxia During One-Lung Ventilation: A Case Report

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ABSTRACT

Anesthetists are concerned about the causes and management of hypoxia during one-lung ventilation (OLV). Here, we report a hypoxic case during OLV and video-assisted thoracic surgery (VATS) for pulmonary lobectomy. The preoperative management of hypertension with amlodipine was considered to be responsible for the hypoxia. As a calcium channel blocker, amlodipine may inhibit hypoxic pulmonary vasoconstriction (HPV) and contribute to the reduction of the ventilation/perfusion ratio (or V/Q ratio). The hypoxia efficiently was treated by atropine, where both tracheal effects and the enhancement of HPV through muscarinic receptor blocking may work. For patients undertaking OLV, the effects of calcium channel blockers as a potential cause for hypoxemia should be paid attention to, where atropine administration may be of clinical benefit.

One-lung ventilation (OLV) generally is used during anesthesia for thoracic surgeries. For OLV, a double-lumen tracheal tube (DLT) is used to realize lung separation in the airway. This technique is essential because it facilitates the surgical performance as well as isolates a healthy lung from the pathologic one. However, there are some concerns for OLV during anesthesia, where hypoxemia is commonly seen.

There are many causes for hypoxemia during OLV. These include, for example, reduced oxygen stores due to the collapse of the non-ventilation lung, ventilation-perfusion mismatch induced by both lateral positions, and decrease in elastic recoil leading to more atelectasis. Accordingly, management of hypoxemia during OLV generally have been applied. Increase fraction of inspiration O_2 (Fi O_2) to 1, double checking the position of DLT, applying positive end expiratory pressure (PEEP), optimizing cardiac output (CO) all have been proven to be effective.

Here, we report an efficiently treated hypoxemia case using atropine during video-assisted thoracic surgery (VATS) for pulmonary lobectomy. Preoperative medication of amlodipine may contribute to the hypoxemia through attenuating HPV during OLV, which may be antagonized by possible HPV augmentation of atropine. Further investigation is therefore suggested.

Received September 9, 2022; accepted October 12, 2022.

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CASE DESCRIPTION

The patient was a 54-year-old woman (166cm, 68kg). She had 10-year hypertension well treated by amlodipine besylate of 5mg/qd and bisoprolol fumarate of 5 mg/qd. Ground-glass opacities (GGOs) were revealed in the anterior segment of the right upper lobe by chest computed tomography (CT) two years before this surgery, during a routine health checkup. She then was treated with close follow up, until a significant change in the size from 6×6mm to 7.6×6.5mm. Then, the VATS for pulmonary lobectomy was decided. Her physical examination revealed no abnormalities and laboratory data were within or close to the normal ranges.

The patient was gently was sedated upon her arrival to the operating room. Blood pressure (BP) of 155/86 mmHg, pulse of 62/min, oxygen saturation (SPO_2) of 96% on FiO_2 21% initially were observed. FiO_2 of 100% was then supplied through facemask, and SPO_2 reached 100% within 5 minutes. A catheter was put into the left radial artery, through which the invasive blood pressure continuously was measured since 158/88 mmHg. Sufentanyl of 1.5ug/kg, propofol of 2mg/kg and vecuronium of 0.6mg/kg sequentially were infused for anesthesia induction. A left-sided DLT of 35F was intubated into the trachea smoothly and properly positioned through fiberoptic bronchoscopy.

Propofol of 4-6mg/kg/h and remifentynl of 0.1-0.2ug/kg/min intravenously were pumped to keep anesthesia state. OLV was initiated right after the skin incision with the vital signs of BP125/76 mmHg, HR 62/min, and SPO_2 100%. The volume-controlled ventilation (VCV) with Lung Protective Ventilation Strategies (LPVS) was used: tidal volume (Vt) 400 mL, frequency (f): 16/min, PEEP 4cmH_2O. The end-tidal carbon dioxide ($etCO_2$) was 32 mmHg. However, airway pressure (Paw) increased from 22 cm H_2O to 35 cm H_2O soon after OLV. Then, the pressure-controlled ventilation (PCV) was used instead of VCV. The inspiratory pressure (insp) was set at 25 cm H_2O and a Vt of 400 to 420 mL was obtained. The inspiratory-to-expiratory ratio (I:E) also was regulated from 1:2 to 1:1.5 to improve dynamic lung compliance. Both frequency and PEEP were kept unchanged. Unfortunately, SPO_2 gradually decreased from 100% to 95% within 5 minutes from the start of PCV.

A series of steps quickly were taken, including suctioning and infusing vecuronium of 20 mg, reconfirming the proper position of DLT with bronchoscopy, insufflating oxygen at 5 L/min continuously into the non-ventilated lung. FiO_2 of 100% remained unchanged all the time. However, SPO_2 continued to fall to 88%. We then increased insp to 28 cm H2O with Vt of 450 to 480 mL, and also regulated frequency to

18/min. The $etCO_2$ fell significantly after these steps from around 32 to 25 mmHg. The SPO_2 increased only slightly from 88% to 89-90%. We noticed a bradycardia of HR 55/min with BP kept at about 125/80 mmHg. Then, atropine of 0.5mg tentatively was infused. Two minutes after injection, HR significantly increased to over 70/min, with a mild change in BP to around 130/80mmHg. Then, both HR and BP fell back within 15 minutes. During this period, SPO_2 increased gradually to 98% within 30 minutes and kept at this level until the end of OLV.

The ventilatory parameters were regulated again: insp 25 cm H_2O and frequency 16/min. Meanwhile, the infusion speed of remifentanyl was reduced from 0.2 down to 0.15ug/kg/min. Under these conditions, HR about 68-75/min, BP around 130/80 mmHg, and $etCO_2$ ranging from 32-35 mmHg all were maintained. Surgery of the left upper lobectomy finally was completed. After the end of surgical procedures, two-lung ventilation was used with VCV and LPVS. SPO_2 increased to 100% quickly then. After extubation, the patient was sent to the post anesthesia care unit (PACU) for further recovery and then smoothly sent back to her ward. She was discharged from hospital 14 days after surgery. No complication was reported during her reexaminations after discharge.

Data listed in Table 1 show the ventilation settings and cardiopulmonary conditions during the early period of OLV, after the performance of series steps, and after the administration of atropine. (Table 1)

DISCUSSION

Hypoxemia is defined as oxygen saturation ($SaPO_2$) of 85% to 90% measured by pulse oximetry for thoracic surgeries. It is closely associated with increased mortality postoperatively [Pannu 2015]. Ventilation-perfusion mismatch is an important cause for hypoxemia during OLV. Both dead space of the collapsed lung and the increased shunt significantly affect the degree of hypoxemia. Therefore, keeping proper ventilation/perfusion ratio (or V/Q ratio) will moderate hypoxemia.

The ventilation-perfusion relationship long has been discussed, where the hypoxic pulmonary vasoconstriction (HPV), a physical protective reflex, is generally known to reduce the anatomical shunt from the perfusion of the independent lung by 40–50% during OLV and thus moderate hypoxia [Lohser 2008]. However, it is a challenge to analyze V/Q or HPV because complicated biological mechanisms are involved. Moreover, both can be influenced by various perisurgical factors.

General anesthesia (GA) may have some effects [Sheybani 2018], but hypoxia does not happen in all patients undertaking GA. This is because other factors, such as changes in cardiac output (CO) and drugs taken for comorbidities, may be more effective on V/Q and HPV. The present case had amlodipine for hypertension management before surgery. As a calcium antagonist, amlodipine is able to block the influx of calcium into pulmonary arterial smooth muscle cells (PASMCs). Moreover, research on both animals and humans has found nifedipine, another calcium antagonist, could dose-dependently reduce HPV [Kennedy 1982; Burghuber 1987]. All suggest further research about the association between calcium antagonist and hypoxia during OLV, as well as reconsideration about the medication of amlodipine before OLV.

There are ways to manage proper V/Q ratio to avoid hypoxia during OLV, most of which were tried by us without significant effect, until atropine was infused. It is known that atropine could inhibit both tracheal secretion and airway contraction by blocking muscarinic receptor (M receptor) to counteract vagal functions, which would benefit the pulmonary ventilation and may also contribute to the improvement of V/Q ratio and SPO_2. During OLV, this tracheal effect might be more significant for limited pulmonary compliance.

The effect of atropine on pulmonary vessels also was reviewed. It was reported that acetylcholine could cause pulmonary vasodilation, during ongoing hypoxic vasoconstriction through the M receptor, which was abolished by atropine pretreatment [Feddersen 1986], indicating that atropine may help to keep the HPV response. To our knowledge, no investigator prospectively has studied atropine as a therapy for augmenting HPV. However, the significant improvement of oxygenation by atropine when conventional techniques fail in the present case strongly suggests further investigation.

In another case, phenylephrine as a α-adrenergic receptor agonist with vasoconstricting properties was found to be beneficial in improving oxygenation during OLV [Schloss 2013], possibly through enhancement of HPV. The impressive improvement in oxygenation by atropine or phenylephrine suggested the importance of accentuating pulmonary vasoconstriction for the augmentation of HPV during OLV, especially when medications, such as calcium antagonist, that

Table 1.

	Vt (mL)	Insp (cmH_2O)	$etCO_2$ (mmHg)	BP (mmHg)	HR (/min)	SPO_2 (%)
OLV	420-450	25	32	115-125/65-80	62-70	88
Pro	450-480	28	25	110-125/65-75	55-70	88-89
Post	450-480	28	25	115-130/70-80	55-75	89-98

OLV, period from the beginning of OLV to the beginning of steps for improving SPO_2; Pro, period of improving SPO_2 before the administration atropine; Post, period after atropine administration until the end of OLV

would attenuate HPV were used. Given the risks of hypoxia faced by patients, as well as the difficulties faced by anesthesiologists, pharmacologic enhancement of HPV during OLV may be of great benefit in clinical practices.

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