■ REVIEW ■

Venous Air Embolism during Surgery, Especially Cesarean Delivery

Venous air embolism (VAE) is the entrapment of air or medical gases into the venous system causing symptoms and signs of pulmonary vessel obstruction. The incidence of VAE during cesarean delivery ranges from 10 to 97% depending on surgical position or diagnostic tools, with a potential for life-threatening events. We reviewed extensive literatures regarding VAE in detail and herein described VAE during surgery including cesarean delivery from background and history to treatment and prevention. It is intended that present work will improve the understanding of VAE during surgery.

Key Words : *Cesarean Delivery; Venous Air Embolism*

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Received : 4 June 2008
Accepted : 27 August 2008

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INTRODUCTION

Venous air embolism (VAE) is the entrainment of air from ruptured veins to the central venous system producing embolism at the right heart or pulmonary artery. In addition, medical gases such as carbon dioxide (1, 2), nitrous oxide (3, 4), nitrogen (5, 6), and helium (7) can also cause or aggravate this condition.

Numerous studies on VAE have been reported in medical or surgical procedures and trauma. Neurosurgery performed in a sitting position has a high risk of VAE, with an incidence of about 76% in posterior fossa surgery (8) but 25% (8) or 7% in cervical laminectomy (9). Whereas, neurosurgical procedures in lateral, supine, or prone positions showed an incidence of 15% to 25% (10). Air embolism occurred in 30% cases of total hip replacement surgery (11). During laparoscopic cholecystectomy, the incidence is reported to be 69% (12). Also, VAE cases associated with central venous catheters (13), endoscopic procedures (14), or inadvertent injection of air as contrast media (15) have been recently reported. Lung (16) or abdominal trauma (17) can also induce VAE.

Cesarean section has also been associated with VAE. The first fatal case of VAE in association with pregnancy was reported in 1850 by Cormack (18). In 1947, Durant et al. (19) indicated for the first time that the uterine sinuses are theoretically vulnerable to the entrance of air, especially in the presence of placenta previa or during manual extraction of the placenta. Until recently, not many cases of massive VAE during cesarean section with devastating morbidity or mortality have been reported (20-28). The incidence of VAE during cesarean delivery ranges from 10 to 97% depending on surgical position or diagnostic tools (Table 1) (29-35). However, it is reported that VAE is responsible for about 1 percent of all maternal deaths (36).

PATHOPHYSIOLOGY, CLINICAL SYMPTOMS AND SIGNS

A vascular access and a gradient between the injury site and the right heart are prerequisites for VAE to occur (37). Factors that determine the severity of VAE include the rate, volume, and duration of air entrapment, patient's position at the time of VAE occurrence, the size of the patient's pulmonary vasculature, type of gas exposure, and the patient's general condition (18, 19). Gravitational gradients from the venous portal of entrance to the right side of the heart as small as 5 cm have been reported to produce entrainment of enough large amounts of air that may embolize the venous pulmonary circulation (10).

The filtering action of pulmonary vessels can protect the systemic and coronary circulation from air emboli derived from the venous circulation (38). Butler and Hills (39) in their studies on dogs reported that the filtration of venous

Table 1. Incidence of air embolism during cesarean section

Authors (reference)	Position of patients	Method of anesthesia	Method of detection	VAE case/total patients (%)	Difference in position
Malinow et al. (29)	LUD	Spinal or epidural	Precordial Doppler	46/89 (52)	–
Fong et al. (30)	Horizontal & LUD	Epidural or general	Precordial Doppler & precordial echocardiogram	14/49 (29)	–
Karuparthy et al. (31)	Horizontal with LUD or 5 to 10° head-up tilt with LUD	Spinal or epidural or general	Precordial Doppler	11/100 (11)	Horizontal 7/50 Head-up 4/50
Fong et al. (32)	Horizontal or 5° head-up tilt	Epidural or general	Precordial Doppler	61/207 (29)	Horizontal 60/134 Head-up 1/73
Handler & Bromage (33)	LUD	Spinal or epidural or general	Precordial Doppler	6/63 (10)	–
Vartikar et al. (34)	LUD	Spinal or epidural or general	Precordial Doppler	51/78 (65)	–
Lew et al. (35)	Horizontal or 10° head-up tilt	General	FEN_2 & precordial Doppler	29/30 (97)	Horizontal 14/15 Head-up 15/15

FEN_2, expired nitrogen concentration; LUD, left uterine displacement; VAE, venous air embolism.

Table 2. The physiological changes, causes, and symptoms and signs of VAE

Cause	Physiologic change	Symptom and sign
Gas exchange abnormality	Decreased PaO_2 Increased $PaCO_2$ Increased (A-a) DO_2 Lung edema	Gasping Dyspnea Cyanosis Hypoxia
Increase in RV afterload Decrease in LV filling	Cor pulmonale RV decompensation Decrease in CO Cardiac arrest	Hypotension Chest pain Murmur EKG change Sudden death

VAE, venous air embolism; RV, right ventricle; LV, left ventricle; EKG, electrocardiogram.

bubbles by the pulmonary vasculature was completed when the air infusion rates were maintained below a threshold value of 0.30 mL/kg/min. Nelson (40) assumed that 500 to 600 mL of air administered in a single rapid injection would be uniformly fatal to human (7 mL/kg) and the required fatal amount would be half (3 mL/kg) if the introduction of air was prolonged for as much as one or two minutes.

VAE may lead to trapping of air bubbles in the pulmonary vessels producing a broad array of physiological changes (Table 2). Gas exchange abnormalities such as decreased PaO_2, increased $PaCO_2$, and an increase in the alveolar-arterial oxygen difference can occur (41, 42). Ventilation-perfusion (V_A/Q) mismatch is the main cause of these abnormalities (43, 44). Increased regions of high V_A/Q contribute to the increase in $PaCO_2$, whereas, decreased PaO_2 results from changes in the intrapulmonary shunt, mixed venous oxygen saturation, and a shift in the distribution of pulmonary blood flow to regions which are relatively overperfused and underventilated (low V_A/Q) (41). Entrapment of venous bubbles in the pulmonary microcirculation may lead to cellular injury and lung edema due to the release of vasoactive mediators (45, 46) and increased microvascular permeability characterized by increased flow of protein-rich lymph (47). This blocking effect of air bubbles and pulmonary artery vasoconstriction due to vasoactive mediators may result in acute cor pulmonale and right ventricular decompensation secondary to the acute rise in right ventricular afterload. Consequently, the preloading of left ventricle and cardiac output can be severely diminished, followed by cardiac arrest (18).

RISK FACTORS

The risk factors for VAE during cesarean delivery are as follows: operation in the Trendelenburg position, abruptio placentae, placenta previa, exteriorization of the uterus, manual extraction of the placenta, severe preeclampsia, antepartum hemorrhage and hypovolemia (18, 22).

DIAGNOSIS

VAE may manifest as chest tightness or short breath with or without hypotension or decreased oxygen saturation in conscious patients undergoing cesarean section under regional anesthesia. In unconscious patients, severe VAE may manifest as acute decrease in end-tidal carbon dioxide ($ETCO_2$), increase in end-tidal nitrogen (ETN_2), hypotension or hypoxia inexplicable by deep anesthesia or hypovolemia. However, other conditions having similar manifestations, such as amniotic fluid embolism, pulmonary thromboembolism, pneumothorax, bronchospasm, pulmonary edema, or myocardial infarction, should also be differentiated.

Table 3. Monitoring systems for detection and evaluation of venous air embolism

Monitoring systems authors (reference)	Positive response	Sensitivity (mL/kg)	Significant reponses (%)	Time to maximam change (sec)	Avail-ability	Invasive-ness	Remarks
TEE							
Furuya et al. (48)		0.02	100		Low	Moderate	Most sensitive, expensive Complications can be possible, even if rare Requires specialist for proper evaluation
Precordial Doppler							
Furuya et al. (48)		0.02	60		Moderate	None	Most sensitive in noninvasive monitoring systems
Furuya et al. (48)		0.05	100				Not quantitative Proper postioning may be difficult in lateral or prone position, or obese patients
ETN$_2$							
Matjasko et al. (53)	>0.02%	0.25/0.5	100/100	39/37	Low	None	If carrier gas is air, useless
Drummond et al. (55)	>0.04%	0.5	50				Requires time to reach steady-state Nitrogen sensitivity of clinical used monitoring is 0.1%, not 0.01%
ETCO$_2$							
Matjasko et al. (53)	>0.2%	0.25/0.5	100/100	106/103	Moderate	None	Widely used, acceptable sensitivity, maybe most useful
Drummond et al. (55)	>0.2%	0.5	66.7				Reflects increased dead space and V/Q mismatch Changes later than TEE, precordial Doppler, ETN$_2$
PAC							
Matjasko et al. (53)	25% of baseline >2 mmHg	0.25/0.5	40/80	144/43	Moderate	High	Invasive, but shows various hemodynamic parameters
Drummond et al. (55)		0.5	33.3				With properly positioned sheath, air aspiration is possible
Oxygen saturation		Low			High	None	Late finding, low specificity, essential monitor in operating room
ECG		Low			High	None	Late finding, low specificity, essential monitor in operating room

TEE, transesophageal echocardiography; ETN$_2$, end-tidal nitrogen; ETCO$_2$, end-tidal carbon dioxide; PAC, pulmonary artery catheter; ECG, electrocardiography.

There has been advancement in monitoring technology contributing to the prevention and treatment of VAE. The ideal monitoring device for VAE in parturients undergoing cesarean section should be sensitive as well as specific for severe or hemodynamically unstable VAE and practically available. Although there is no such ideal monitoring device yet, the proper selection of a monitoring device considering the operation and medical condition of the patient is helpful to detect and diagnose VAE in time for prevention and treatment. In Table 3, each monitoring system is listed in order of sensitivity, their characteristics summarized and compared.

Transesophageal and transthoracic echocardiography

Transesophageal echocardiography (TEE) is relatively invasive but is the most sensitive device for monitoring air embolism. TEE enables to detect a bolus dose of air as small as 0.02 mL/kg (48). Because it is easy to secure the probe at the selected position for a long period, continuous images can be obtained for a relatively long time without intervention compared to transthoracic echocardiogram (TTE). TTE, however, has the advantage of noninvasive examination. TEE and TTE have the advantage of being able to detect paradoxical air embolism, intracardiac defects and evaluate intravascular volume status (48, 49). The echocardiogram is useful to identify the route of air emboli entrained and classify severity of air embolism (Table 4, Fig. 1) (12). In massive air embolism detected by TTE, hyperdynamic left ventricular function with a dilated right ventricle, dilated right ventricular outflow tract and pulmonary artery, and decreased right ventricular function were observed, but no air was found initially (13). In repeated TTE imaging, a large influx of air filling the right heart and pulmonary artery was demonstrated (13). However, the majority of VAE cases in cesarean section are not fatal and have no adverse sequelae despite its high incidence (29-36). TEE is less available than other monitoring devices since it is expensive and requires a well-trained and certified echocardiographer or anesthesiologist for proper and continuous monitoring (50).

Precordial Doppler ultrasound

Precordial Doppler ultrasound is considered efficacious and favored for the surveillance of air embolism for its simplicity, noninvasiveness, and being almost as sensitive as TEE (51). It can detect a bolus dose of air as small as 0.05 mL/kg with immediate alterations in the ultrasonic pattern (48). Because this device produces a sound resembling a "washing

Table 4. The stage of VAE detected with TEE

Stage	TEE
0	No emboli in RA, RV and RVOT
I	Single gas bubbles in RA, RV and RVOT
II	Gas emboli filling less than half the diameter of RA, RV and RVOT
III	Gas emboli filling more than half the diameter of RA, RV and RVOT
IV	Gas emboli completely filling the diameter of RA, RV and RVOT

RA, right atrium; RV, right ventricle; RVOT, right ventricular outflow tract; VAE, venous air embolism; TEE, transesophageal echocardiography.

machine" or "drum", it is easy to distinguish among other alarm sounds and to monitor air embolism while tending to other duties of patient care. It is worth pointing out that a positive Doppler signal does not always indicate clinical significance because hemodynamically significant air embolisms during caesarean section are rare and audible Doppler signals are sometimes false-positive (35).

Proper positioning of the precordial Doppler probe over the anterior chest wall is crucial for early and exact detection of venous air embolism, especially in obese patients or parturients (52). To increase the sensitivity and specificity of precordial Doppler, the right sternal border over the right heart has been recommended as the ideal position of the Doppler probe. However, placing the probe over the left sternal border has also been used (52). Normal saline or carbon dioxide may be injected to verify proper positioning of the precordial Doppler probe.

Pulmonary artery catheter

The pulmonary artery catheter is less sensitive than TEE, precordial Doppler ultrasound, or gas-sensing methods but
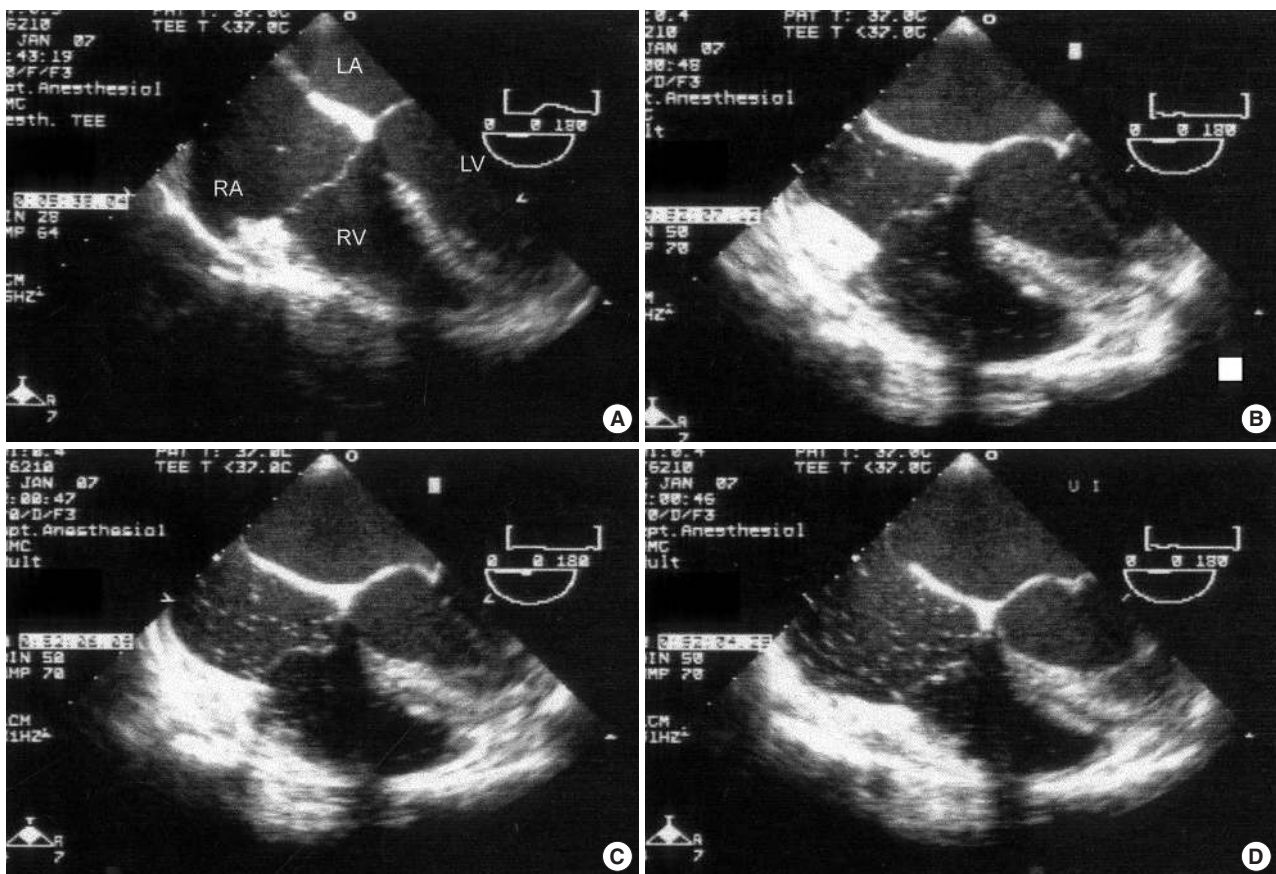
Fig. 1. Venous air embolism detected by transesophageal echocardiography (mid-esophageal four-chamber view) during cesarean delivery in our recent study. (A) grade I, (B) grade II, (C) grade III, (D) grade IV.
RA, right atrium; RV, right ventricle; LA, left atrium; LV, left ventricle.

the most invasive way among the monitoring devices mentioned in related articles. The pulmonary artery catheter is capable of detecting as little as 0.5 mL/kg of air in 80% of bolus injections when pulmonary artery pressure exceeding baseline by 25% is defined as a positive sign of VAE (53). Although the pulmonary artery pressure is less sensitive than $ETCO_2$, it changes earlier than $ETCO_2$, when air embolism occurs as much as volumes of 1.5 mL/kg (53). The pulmonary artery catheter has limitations in detecting VAE in normal patients undergoing elective cesarean section due to its invasiveness. However, in patients with other complicated indications requiring its use, the pulmonary artery catheter can provide useful information such as pulmonary artery hypertension, low cardiac output and low mixed venous saturation that manifests in severe or fatal VAE (53).

ETN_2 monitor

The most sensitive method of VAE detection among gas-sensing methods is the ETN_2 monitor. Increased ETN_2 in a patient ventilated with denitrogenated gas has been considered as a specific sign of venous air embolism (54). ETN_2 monitor is capable of detecting as little as 0.25 ± 0.5 mL/kg of air (53, 55) and increases rapidly after an experimental VAE is large enough to cause minimal changes in blood pressure (56). The time to maximal change in ETN_2 (32 ± 8 sec) was 30-60 sec earlier than that of pulmonary artery catheters and $ETCO_2$ (53). The mass spectrometer used in the study by Matjasko et al. (53) had a nitrogen sensitivity of 0.01%, in contrast to the 0.1% in clinically used mass spectrometers. Emission spectrometry can also be used to detect increased ETN_2 levels indicative of venous air embolism as an alternative to mass spectrometers, and may be a more sensitive detector (0.1 mL/kg) (54).

$ETCO_2$ monitor

$ETCO_2$ is a convenient and useful tool to detect VAE because of its common use in the operating room. Although $ETCO_2$ is as sensitive as ETN_2, it changes later than ETN_2. A change in $ETCO_2$ is considered significant and can be detected if it drops 0.2% (53) or 2 mmHg (57) below the baseline. Despite its clinically practical advantages, $ETCO_2$ monitoring has drawbacks. It can be affected by other factors such as airway obstruction, systemic hypotension and reduced cardiac output which decrease specificity and reliability. Also, because secure airway and ventilation are required for reliable gas-sensing monitoring, gas-sensing methods like ETN_2 and $ETCO_2$ cannot be applied to patients undergoing regional anesthesia for cesarean section.

Pulse oximetry, electrocardiography (ECG)

These monitoring systems display the late findings of VAE, detecting the complications of VAE and severe physiologic deterioration caused by V_A/Q mismatch, right and/or left heart failure, or paradoxical arterial air embolism (13, 34, 58). Therefore, these methods are not suitable for the early detection of VAE, especially in patients under general anesthesia without N_2O, and negative findings do not guarantee the absence of VAE.

The ECG changes during cesarean delivery were known to be nonspecific signs of VAE probably caused by hormonal influence, tachycardia, or patient position (58, 59). However, these monitoring systems are available in the operating room and are familiar to most anesthesiologists. ECG changes such as ST depression or elevation, widened QRS complex, premature ventricular contraction or T wave change, are generally shown as the consequence of severe physiologic deterioration in large or rapid air entrainment (13, 60).

Pulse oximetry has low sensitivity for detecting VAE but it is also important for patient safety. Williamson et al. (60) reported the first primary means for detection of VAE is a fall in $ETCO_2$ (34% of 38 VAE cases) and the second one is desaturation (26% of 38 VAE cases).

PREVENTION

Position

It has been accepted that the 15° left lateral tilt position may increase the risk of VAE during cesarean section, due to a subatmospheric venous pressure gradient between the right atrium and uterine incision (31). In addition, a trendelenburg position or exteriorization may augment the pressure gradient and increase the risk of VAE, because the right atrium is positioned below the uterus (24, 37). A strategy to increase right atrium pressure (RAP) is rational when its physiologic effect is considered carefully. To reverse the subatmospheric venous pressure gradient, the effect of patient positioning has been investigated. The effect of a 5-10° reverse trendelenburg position on the incidence of VAE is controversial. In a case-control study conducted on 100 healthy patients undergoing cesarean section, there was no difference in incidence between the supine and 5-10° reverse trendelenburg position with a 15° lateral tilt (31). However, other investigators reported that the application of a 5° reverse trendelenburg position dramatically decreased the incidence of VAE from 44% to 1% (32).

Positive end-expiratory pressure (PEEP)

PEEP is known to be effective in preventing VAE by increasing venous pressure at the level of incision. However, PEEP does not decrease the incidence of VAE but rather have adverse effects on the cardiovascular system such as lowering cardiac output and increasing pulmonary vascular resistance in pati-

Table 5. The management of VAE

Inform the surgeon
Adequate hydration
Prevent further gas entry
Flood the surgical field
Evaluate and remove the origin of gas entry
Increase right atrial pressure and trap the air in right atrium
Reverse trendelenburg position, if possible
Left lateral recumbent position
Discontinue N₂O and ventilate with 100% oxygen
Central venous catheterization: proper position for aspiration of air
Resuscitation
Fluid administration
Durgs:
Inotropes
Vasopressor
Vasodilator specific to pulmonary circulation
Cardiopulmonary resuscitation
Hyperbaric oxygen therapy

VAE, venous air embolism.

ents in sitting positions for neurosurgery (61). However, in a supine position, PEEP does increase pulmonary vascular resistance and the incidence of paradoxical air embolism although it may lower cardiac index (61). Because PEEP up to 10 cmH₂O does not alter the pulmonary arterial wedge pressure (PAWP) - RAP difference, it can be safely applied without the concern of paradoxical arterial embolism (62). Although applying PEEP up to 10 cmH₂O may not be harmful in patients undergoing cesarean delivery, no benefit to overcome a potential harm has been found yet. Furthermore, sudden release of PEEP to 0 mmHg can lead to VAE and the Valsalva maneuver can increase the incidence of paradoxical arterial embolism (63).

Military anti-shock trousers (MAST) suit

MAST suit can increase RAP dramatically, inflated up to 40 mmHg in the lower compartment and 30 mmHg in the abdominal compartment (64) and its effect is potentiated with PEEP (64, 65). However, MAST suits may not be effective because the increase in filling pressure is only transient in half of the patients (66, 67). In addition, MAST suits may accompany complications such as nerve injury or ischemia in lower extremities and decreased vital capacity (66, 67). Due to these collateral complications, use of MAST is discouraged in cesarean section.

Treatment of severe VAE (Table 5)

The goals of management when severe VAE is suspected or manifested, are prevention of further gas entry, removal of entrained gas, and maintenance of hemodynamical stability.

Strategies accepted to minimize the entry of gas include flooding the surgical field and increasing RAP. When VAE

is diagnosed and hemodynamic deterioration is manifested, the anesthesiologist has to inform the surgeon and the surgeon should flood the surgical field with fluid such as normal saline and eliminate any origin of gas entry if possible. It has been recommended to reposition the patient thus to increase RAP and to trap the air in the right atrium. In patients undergoing cesarean section, placing the patient in a reverse Trendelenburg position mandates close monitoring, because the position can aggravate hemodynamic instability. Placing the patient in a Trendelenburg position for central venous catheterization or hemodynamic support may increase the negative pressure gradient thereby increasing gas influx even further. Therefore, the surgical field should be flooded before positioning. Placing the patient in a left lateral recumbent position may be helpful for trapping and aspirating gas entrained in the right atrium and preventing and relieving the air-lock in the right heart (68). Geissler et al. (69), however, demonstrated that VAEs of lesser degree (2.5 mL/kg at a rate of 5 mL/sec) did not result in significant differences of hemodynamics and outcome between the right lateral recumbent position and left lateral recumbent position. Despite these results, groups in the left lateral position demonstrated repositioning of the VAE to the right atrium and tricuspid area on the echocardiogram (69).

When VAE is suspected, nitrous oxide should be discontinued because ventilation with nitrous oxide expands pulmonary vascular bubbles and increases the residual time of VAE leading to aggravation of the hemodynamic consequences (65, 70-73). Also, the patient should be ventilated with 100% oxygen in order to wash out entrained air and to improve V/Q mismatch and hypoxemia. Fortunately, the development of various anesthetic agents has discouraged the use of nitrous oxide, especially in procedures with a high risk of VAE.

If a central venous catheter or pulmonary artery catheter is placed, the trapped air in right atrium (RA), right ventricle (RV), or right ventricular outflow tract (RVOT) can be aspirated. In patients with risk factors for VAE and massive hemorrhage, central catheterization prior to induction should be considered. When the central venous catheter is properly positioned, up to 50% of the entrained air can be aspirated and using a multi-orifice catheter is helpful (74). The proper position of the catheter tip is 2 cm below the superior venalright atrial junction and can be verified by chest radiography or ECG attached to the catheter (75).

Hemodynamics may be deteriorated by right ventricular failure caused by the air-lock of entrapped air bubbles in the right heart, pulmonary artery vasoconstriction due to vasoactive mediators, and subsequent left ventricular failure due to severely diminished left ventricular filling. Maintenance of coronary perfusion pressure is essential to prevent further deterioration of the right ventricle and to improve right ventricular function (76). Norepinephrine can significantly improve ventricular performance without constricting either the pulmonary or renal circulation (77, 78). Use of vasodila-

tor for the treatment of increased pulmonary vasoconstriction and reduction of right ventricular afterload can be attempted with care when hypotension is not present (76). Prostaglandin analogue or phosphodiesterase inhibitors may be considered to treat severe pulmonary hypertension and to reduce right ventricular afterload (79). Milrinone or dobutamine may provide inotropic support and decrease the right ventricular afterload (80).

Severe and fatal VAE can lead to a cardiac arrest following dysrhythmias such as premature ventricular complex, widened QRS wave, or ventricular tachycardia. Cardiopulmonary resuscitation should be performed with drugs such as epinephrine or atropine according to the Advanced Cardiac Life Support protocol. External cardiac compression may contribute to the breakup of the locked air and its transit into pulmonary circulation (38, 39).

Hyperbaric oxygen therapy has been reported to be useful in VAE, especially for neurologic deficits caused by cerebral air embolism (81-83). The effect of hyperbaric oxygen therapy is based upon reduction of the bubble size by accelerated resorption of nitrogen and increased delivery of oxygen to ischemic brain tissue (83).

CONCLUSIONS

We reviewed extensive literatures regarding VAE in detail and herein described VAE during surgery including cesarean delivery from background and history to treatment and prevention. It is intended that present work will improve the understanding of VAE during surgery, especially cesarean delivery.

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