End tidal carbon dioxide (ETCO2) and peripheral pulse oximetry (SpO2) trends and right-to-left shunting in neonates undergoing non cardiac surgery under general anesthesia

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Abstract

Pulse-oximetry and capnography monitoring has improved the safety of anaesthesia. Using two case-reports we illustrate how trends in combined and concurrent pulse oximetry and capnography can assist diagnosis and management of acute right-to-left shunts in neonates undergoing non-cardiac surgery under general anaesthesia. In both cases, rapid desaturation was the dominant sign resulting from right-to-left blood flow at the level of the patent ductus arteriosus and/or functionally opened foramen ovale (reversing the preoperative left-to-right shunt). The concurrent hypercarbia detected in arterial blood gas was significant but possibly not evident in ETCO2 because only a small proportion of systemic venous blood reached the pulmonary circulation for gas exchange.

Treatment methods included improving oxygenation by increasing inspiratory oxygen concentration (FiO2), volume expansion to improve pulmonary blood flow, reduction of CO2 by hyperventilation and increasing the dopamine infusion dose in one infant to augment systemic vascular resistance.

In the event of a reversed left to right shunt, pulmonary arterial blood CO2 (PaCO2) rises as a result of systemic recirculation. However, a rise in ETCO2 depends on the remaining pulmonary blood flow. For example, if the reversed shunt is large (i.e. increasing right to left shunt), then pulmonary blood flow is reduced and the CO2 delivered to the lungs per unit time becomes inadequate to reflect it in expired breaths as ETCO2. Therefore, ETCO2 can be low in a suddenly reversed shunt state. Poor pulmonary blood flow leads to a low CO2 elimination in expired air resulting in a low ETCO2 record.

Keywords: Neonate, reversed intra-cardiac shunt, capnography, peripheral oxygen saturation, general anaesthesia.
Introduction
Several decades ago, the first sign of hypoxia under anaesthesia was cyanosis [1]. With the use of pulse-oximetry, hypoxia was recognisable before the onset of cyanosis. This led to a step-change in the safety of anaesthesia [2]. Capnography provided an additional safeguard by detecting airway issues before the onset of desaturation [3].
Interpretation of concurrent pulse oximetry and capnography further enhanced the detection and understanding of complex clinical scenarios: for example partial airway obstruction, pulmonary embolism, and oesophageal intubation [4] [5].
A rise in end-tidal carbon dioxide (ETCO$_2$), with concurrent desaturation was recently described in reversal of intra-cardiac shunt [6]. In this report, we describe a sudden intraoperative reduction in ETCO$_2$ with the reversal of intra-cardiac shunts in two neonates undergoing non-cardiac surgery.
In addition, we discuss the role of ETCO$_2$ and peripheral pulse oximetry (SpO$_2$) in the clinical diagnosis, potential intraoperative triggers, and immediate treatments of this life-threatening scenario.
Case report 1
A 6-day old, 640g neonate, born at 25-week gestation and ventilated since birth required an urgent laparotomy for a suspected intestinal perforation. She was on positive pressure ventilation (FiO$_2$ 40%, respiratory rate 55 per minute, peak inspiratory pressure (PIP) 20cm H$_2$O and positive end expiratory pressure -PEEP 5cm H$_2$O). She was also requiring inotropic support with both dopamine and dobutamine each at 10 mcg/kg/hr. There was a right-sided pneumothorax with an intercostal drain in-situ. An Echocardiogram demonstrated a patent ductus arteriosus with normal cardiac anatomy.
Anaesthesia was induced and maintained with sevoflurane in oxygen and air, together with fentanyl and atracurium boluses, and continued inotropic support. During surgery, an episode of significant desaturation was noted immediately following a transfusion of 10mls of packed red cells. This was associated with a concurrent reduction of ETCO$_2$ (Figure 1).
Air embolism was considered unlikely as no air bubbles were seen in the intravenous access lines. An arterial blood gas showed a mixed respiratory acidosis (pH 7.11, PaCO$_2$ 10.9 kPa, PaO$_2$ 7.7 kPa, BE -4.9 and Standard HCO$_3$ 20.9 mmol/l) with a concurrent end-tidal ETCO$_2$ of 2.8 kPa. The blood transfusion was stopped, dopamine increased to 20mcg/kg/min and the inspired oxygen concentration was increased to 97%. The patient’s oxygen saturations improved dramatically, and simultaneously the PaCO$_2$ returned towards normalcy (Figure 1 - Case 1).

Case report 2
A 38-week neonate was delivered by elective caesarean section for urgent surgery of an antenatally diagnosed meningo-myelocele. At 2 hours of age she was in the operating theatre self-ventilating room air whilst recording a variable peripheral SpO2 of 85-95%. She was not noted to have any other congenital abnormalities. The heart was reported normal in the antenatal scans.
Anaesthesia was induced with sevothflurane in oxygen and air, together with fentanyl and atracurium boluses for intubation. Immediately after induction, a reduction of ETCO$_2$ was noted with an associated reduction in SpO$_2$. A bolus of fluid (20mls of Hartmann’s) was given.
and FiO₂ was increased to 100%. The SpO₂ recovered and ETCO₂ also increased (Figure 1- Case 2). An arterial blood gas at this time showed a pH 7.21, PaCO₂ 8.8 kPa, PaO₂ 26.7 kPa, BE -3.0 and a concurrent end-tidal (ET) CO₂ of 4.5 kPa.

Both neonates returned to neonatal intensive care in stable condition. They both made good clinical progress following surgery.

**Discussion**

Although a rise in ETCO₂ has been described in reversal of left-to-right cardiac shunts [6], in this report we conversely observe a reduction of ETCO₂.

We discuss possible explanations for a large discrepancy between ETCO₂ and PaCO₂, and triggering mechanism that led to the reversal of shunts. We also explain the rationale for rectifying measures undertaken, both physiological and pharmacological in these two neonates presenting with sudden intra-operative right-to-left-shunts.

**The role of ET CO₂ and PaCO₂**

The arterial-alveolar tension gradient for CO₂ has been investigated in normal new-born infants and in sick neonates as early as in 1962. Normal infants had virtually no PCO₂ gradient from pulmonary capillary to alveolus, whereas in sick infants an average difference observed was 13.9 mm Hg. This gradient for PCO₂ was considered to be a consequence of increased alveolar i.e. physiological dead space, largely due to poor perfusion of ventilated alveoli. In severely ill infants more than 60% of ventilated alveoli appear to be under-perfused [7]. What we have demonstrated in this report is a comparable situation of a larger dead space created by reduced pulmonary blood flow following a reversed left to right shunt.

Low pulmonary blood flow during right-to-left shunting is recognized. For example, cardiac catheterization data in neonates with transitional circulation has shown sluggish radio opaque dye movement in the pulmonary circulation when there is right-to-left intra-cardiac shunting via the foramen ovale and ductus arteriosus [8]. Since blood gases during cardiac catheterisation was masked with therapeutic interventions such as bicarbonate therapy, interpretation of ETCO₂ had been difficult in the past [8]. This was not so in our cases as no interventions were made that could directly interfere with the interpretation of blood gases.

In both our cases the ETCO₂ was markedly lower than PaCO₂ in association with a lower SpO₂. Our interpretation was that the systemic desaturation was due to reversal of blood flow at the level of the patent ductus arteriosus and/or concomitant right to left flows across a functionally open foramen ovale, the so-called transitional circulation. The desaturation and hypercarbia was related to relative separation of the two circulations with systemic recirculation of increasingly hypoxic and hypercarbic blood (Figure 2).

![Figure 2. A schematic diagram of 'systemic re-circulation' leading to hypercarbia and desaturation. Lower ETCO₂ was due to proportionality low pulmonary blood flow.](image)
A rise in ETCO₂ and a reduction in SpO₂ with reversal of L-R shunts in neonates results from accumulation of CO₂ in the systemic circulation due to newly established ‘systemic re-circulation’ following the reversal of the left to right shunt [6]. In our cases a high arterial CO₂ and a reduced CO₂ was detected in the expired gas. This is because only a small proportion of the systemic venous blood was able to reach the pulmonary circulation for gas exchange. Thus, a reversed left to right shunt can lead to a spiral decline with worsening hypoxia and rising pulmonary vascular resistance, diverting more blood away from the lungs.

The reduction in ETCO₂ was possibly related to pulmonary blood flow that was proportionately too low to establish adequate gas exchange. We propose that a reduction of ETCO₂ can also be a presenting feature in a reversed left to right shunt situation mimicking pulmonary embolism.

During the recovery phase, with the improvements in oxygenation, a rise in ETCO₂ was noted before it would plateau to pre-event levels. This is because with a large left to right shunt reversal, there is a build-up of CO₂ in the systemic circulation that would be released to alveolar gas with the re-establishment of the pulmonary circulation. The diagnosis of a reversed shunt using the above clinical features is swift and this will help clinicians to ameliorate such a situation before serious decompensation occurs.

In literature, end-tidal CO₂ monitoring in neonatal intensive care is described as less precise than transcutaneous monitoring. Therefore, it was considered only useful for trending [9]. It was not a substitute for direct PaCO₂ analyses in preterm infants [10] or in severe chronic pulmonary disease [11].

This discrepancy between PaCO₂ or transcutaneous CO₂ and ETCO₂ can be explained by variable shunt flows that may have co-existed in these neonates that have not been taken into account in the above investigations. However, the value of capnography trending in neonatal anaesthesia is overwhelming as demonstrated in our cases. For this purpose, sampling methods i.e. distal side stream vs mainstream is no bar [12].

We have described in these case reports how intracardiac shunting direction change creates a major gap between ETCO₂ and PaCO₂. We have also shown how we can use the widening PaCO₂-ETCO₂ gap resulting from a rise in PaCO₂ and a fall in ETCO₂ especially associated with a reducing SpO₂ to suspect a reversal of a shunt or re-establishment of a foetal circulation. Since PaCO₂-ETCO₂ gap has been shown to be consistently reliable in the same individual [13], PaCO₂-ETCO₂ gap may have a value for gauging the proportion of intracardiac shunting in the neonatal intensive care set-up where direct measurement of shunt flow by Doppler is not practical with the currently available instruments.

Potential triggers of sudden intraoperative right-to-left shunts

What we have demonstrated in our cases is a situation mimicking persistent foetal circulation under anaesthesia. The triggers we observed in one patient was blood transfusion and anaesthetic induction agents in the other.

Why can shunting suddenly be reversed under general anaesthesia? One known mechanism is lowering of systemic vascular resistance (SVR) leading to lowered systemic blood pressure and reversed pressure gradient at shunt level. This was the most likely mechanism in case 2. In case 1, however, the reversed shunt status was triggered by a blood transfusion whilst the patient was also on vasopressors. The most plausible explanation is a rise in pulmonary vascular resistance (PVR) reversing the pressure gradient shunt level. This mimics persistent foetal circulation in neonatal intensive care.

Ten millilitres of blood constituted 15-20% of blood volume in this neonate. This could have introduced a significant change in HbF: HbA ratio leading to a situation of poor oxygen release due to two reasons. Firstly, HbA is inherently poor in release of oxygen at tissue level with small changes on oxygen tension when compared to HbF. Its known that HbA increases right shift
of the oxygen dissociation curve, resulting in less affinity of oxygen in HbA, thus facilitating oxygen release and oxygenation in the pulmonary circulation. It also shown that in extremely premature neonates (< 27 weeks) the mean Pₕ₀ prior and after transfusion of 26.9 mL/kg of packed red cells was 18.5±0.8 and 21.0±1 mm Hg (P=.0003) while the mean percentage of HbF was 92.9±1.1 and 42.6±5.7%, respectively [14]. In maternal blood Pₕ₀ was estimated as 30.1mm Hg whereas in the normal new-born it was 22.9 mm Hg. Pₕ₀ rises with addition of 2,3 DPG in vivo [15]. However, HbF with an extreme left shift oxygen dissociation curve, is designed to capture oxygen at a very low level in the placenta and release a large amount in foetal tissue even with a small reduction in oxygen tension. It is this capability for a large volume oxygen release that would be lacking when HbF is suddenly proportionately replaced with HbA in the sick neonate. Secondly stored blood with depleted 2, 3 DPG, further reduce ability for HbA to release oxygen, due to a left shift of the oxygen-haemoglobin dissociation curve. This sudden change of oxygen dissociation curve mechanics could have led to a rapid decline in amount of oxygen available at tissue level, in particular at the pulmonary circulation leading to pulmonary vasoconstriction and a rise in pulmonary vascular resistance (PVR) despite HbA increasing the Pₕ₀. This could have triggered the reversed shunt by altering pressure gradients at shunt level.

Management in neonates with sudden intraoperative right-to-left shunts

Intraoperative sudden left-to-right shunts respond commonly to volume and increase in systemic vascular resistance [16] [17]. Our treatment strategies were similar, both physiological and pharmacological. The physiological methods included hyperventilation, high oxygen therapy and volume expansion. This was to promote pulmonary vasodilatation and systemic vasoconstriction. On the other hand, the use of systemic vascular constric- tor pharmacologically was useful to rapidly reduce a re-versed shunt to a normal left to right shunt. These manoeuvres reduce right to left shunting by altering the pressure gradients between left and right heart chambers. Dopamine was useful in one infant. In situations of transitional circulation, dopamine infusion has been shown to be successful therapy. It mitigates myocardial dysfunction associated with transitional circulation [18]. It may have also increased SVR although was not reported [18].

In case 1, the situation was remedied by stopping the blood transfusion (the probable trigger), improving oxygenation, and the increase in the inotrope/vasopressor dose. These manoeuvres were expected to reduce the pulmonary circulation pressure and also increase systemic vascular resistance and reduce the reversed pressure gradients at the foramen ovale or patent ductus. This promoted the re-establishment of pulmonary blood flow leading to recovery of ETCO₂ and improved oxygenation (Figure 1).

In our case 2, desaturation responded well to fluids and 100% oxygenation. These manoeuvres would have reduced pulmonary vascular resistance and increased systemic vascular pressure improving the situation by reducing the reversed shunt flow at PFO or PDA.

Conclusions

We have demonstrated how the circulation in neonates can become easily unbalanced during non-cardiac anaesthesia by induction of general anaesthesia or by a blood transfusion, resulting in the lowering of SVR by anaesthetics agents, and a rise in PVR, respectively. The clinical consequences of an acute right-to-left shunt intraoperatively can be devastating. We have shown how this can be diagnosed and managed with relatively simple non-invasive capnography and pulse oximetry monitoring.

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References