Clinical Reports

Profound hypoxemia during treatment of low cardiac output after cardiopulmonary bypass

Kevin C. Dennehy MB BCH FFARCSI,
Jean-Yves Dupuis MD FRCPC,
Howard J. Nathan MD FRCPC,
J. Earl Wynands MD FRCPC

Purpose: To illustrate the multiple causes of hypoxemia to be considered following cardiopulmonary bypass and how therapy given to improve oxygen delivery may have contributed to a decrease in arterial oxygen saturation to life-threatening levels.

Clinical features: A 61 yr old man with severe mitral regurgitation and chronic obstructive lung disease underwent surgery for mitral valve repair. A pulmonary artery catheter with the capacity to measure cardiac output and mixed venous oxygen saturation (SvO_2) continuously was used. Two unsuccessful attempts were made to repair the valve which was finally replaced, requiring cardiopulmonary bypass of 317 min. Dobutamine $5 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ and sodium nitroprusside $1 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ were used to increase cardiac output. Soon after, the SvO_2 decreased progressively from 55 to 39%. The patient became cyanotic with a PaO_2 of 39 mmHg. Sodium nitroprusside was stopped and amrinone 100 mg bolus followed by $10 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ was given in addition to adding PEEP to the ventilation. With these measures PaO_2 could be maintained at safe levels but PEEP and high inspired oxygen concentrations were needed postoperatively until the trachea could be extubated on the third postoperative day.

Conclusion: The profound hypoxemia in this case was likely due to a combination of intra- and extrapulmonary shunt, both augmented by sodium nitroprusside. The desaturation of mixed venous blood amplified the effect of these shunts in decreasing arterial oxygen saturation. The interaction of these factors are analyzed in this report.

Objectif : Illustrer les multiples causes de l'hypoxémie dont il faut tenir compte après une circulation extracorporelle et montrer comment la thérapie qui vise à améliorer la livraison d'oxygène peut avoir contribué à baisser la saturation artérielle en oxygène à des niveaux dangereux.

Aspects cliniques : Un homme de 61 ans souffrant de régurgitation mitrale sévère et de bronchopneumopathie chronique obstructive devait subir une chirurgie réparatrice de la valvule mitrale. On a utilisé une sonde artérielle pulmonaire, ayant la capacité de mesurer de façon continue le débit cardiaque et la saturation en oxygène du sang veineux mêlé (SvO_2). La réparation ayant été tentée deux fois sans succès, on a finalement remplacé la valve, ce qui a nécessité 317 min de circulation extracorporelle. Pour augmenter le débit cardiaque, on a administré $5 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ de dobutamine et $1 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ de nitroprussiate de sodium. Peu après, la SvO_2 a diminué progressivement de 55 à 39 %. Le patient est devenu cyanosé et présentait une PaO_2 de 39 mmHg. Le nitroprussiate de sodium a été stoppé et on a administré un bolus de 100 mg d'amrinone suivi de $10 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ en plus de l'addition d'une PEP à la ventilation. Ces interventions ont permis de maintenir la PaO_2 à des niveaux de sécurité, mais la PEP et de fortes concentrations d'oxygène inspiré ont été nécessaires après la chirurgie jusqu'à ce que l'extubation de la trachée soit possible le troisième jour postopératoire.

Conclusion : Dans ce cas, l'importante hypoxémie était probablement causée par une combinaison de shunts intra et extrapulmonaire qui ont été accentués par le nitroprussiate de sodium. La désaturation du sang veineux mêlé a amplifié l'effet de ces shunts en diminuant la saturation artérielle en oxygène. L'interaction de ces facteurs est analysée dans l'article qui suit.

From the Department of Cardiac Anesthesia, University of Ottawa Heart Institute, HIRC, H341, 1053 Carling Ave., Ottawa, Ontario, Canada K1V 9H2.

Address correspondence to: Dr. Howard Nathan, Phone: 613-761-4775; Fax: 613-761-4734.

Accepted for Publication October 22, 1998

CARDIAC output (CO) and oxygen delivery often require optimization immediately after cardiopulmonary bypass (CPB). However, the therapeutic approaches currently available to achieve these goals may be associated with detrimental side effects. The following case report describes a patient who, after mitral valve surgery, developed profound mixed venous oxygen desaturation followed by acute life threatening hypoxemia during treatment of low CO with dobutamine and sodium nitroprusside (SNP).

Case report

A 61 yr old man with severe mitral regurgitation (MR) was admitted electively for mitral valve repair. At the time of admission, his symptoms included dyspnea on minimal exertion, two pillow orthopnea and paroxysmal nocturnal dyspnea. He also had a chronic, productive cough and a history of heavy smoking (50 pack years). Cardiac medication included 20 mg nifedipine twice daily for hypertension and 40 mg furosemide once daily. Physical examination revealed no jugular venous distention and no ankle edema. Auscultation of his chest revealed fine bibasilar crackles and a pansystolic heart murmur, grade 4/6, radiating to the axilla. Hematological studies and a routine chest radiograph were within normal limits. An electrocardiogram showed normal sinus rhythm with right bundle branch block. Transesophageal echocardiography revealed severe mitral regurgitation due to myxomatous degeneration as well as a patent foramen ovale with a resting left to right shunt. Heart catheterization demonstrated the presence of severe MR and normal coronary arteries. The cardiac index (CI) was $2.4 \text{ l}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$, the pulmonary artery (PA) pressure was 63/25 mmHg, the PA occlusion pressure (PAOP) 22 mmHg, and left and right ventricular end diastolic pressures were 18 and 19 mmHg, respectively. The contractile state of the left ventricle was considered to be normal.

In the operating room a PA catheter connected to a monitor (Vigilance™ Monitor, Baxter Healthcare Corp., Irvine, Ca, USA) with the capacity to record CO and mixed venous oxygen saturation (SvO_2) continuously was inserted following induction of anesthesia. The PA pressure at that time was 60/28 mmHg and the CI $2.4 \text{ l}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$. The mitral valve was repaired and CPB terminated uneventfully. Transesophageal echocardiography (TEE) performed shortly after separation from CPB revealed the persistence of severe MR. Cardiopulmonary bypass was resumed and a mitral valve annuloplasty was performed. Following this, CPB was terminated with the patient receiving 5

$\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ dobutamine. A TEE study performed at this time revealed that the MR had worsened and a mitral valve replacement (MVR) was performed. The CPB time was 317 min and the cross clamp time was 163 min. Separation from CPB for the third time was initially uneventful using $5 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ dobutamine. The continuous CO monitor measured a CI of $1.9 \text{ l}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$ confirmed by the bolus injectate technique. The SvO_2 was between 50 - 55%. The systemic blood pressure was 105/55 mmHg and the systemic vascular resistance (SVR) was $1600 \text{ dyn}\cdot\text{sec}\cdot\text{cm}^{-5}$. The patient bled excessively and eight units of platelets, six units of fresh frozen plasma and ten units of cryoprecipitate were administered. As the blood products were given the blood pressure (BP) increased to 150/80 mmHg. An infusion of SNP was commenced at $1 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ to control BP and improve CI. The BP decreased to 120/70 mmHg, the SVR to $940 \text{ dyn}\cdot\text{sec}\cdot\text{cm}^{-5}$ and the PA pressure remained at 50/30 mmHg during the infusion. The CI increased to $2.3 \text{ l}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$. Despite this hemodynamic improvement the SvO_2 decreased from 55 to 45% (Figure 1). The reason for the decreased SvO_2 could not readily be explained by the treating physicians. However, as the hematocrit was only 21% (Table), packed red blood cells were transfused with the intention of increasing oxygen delivery (DO_2). Despite this intervention the SvO_2 continued to decrease to as low as 39%. The PA temperature measurements were steady at 37.2°C . Neuromuscular monitoring of the periorbital muscles revealed no twitch in response to train-of-four stimulation. The patient's arterial oxygen saturation (SaO_2) as recorded by pulse oximetry, remained $>95\%$. Doubts were expressed regarding the validity of the SvO_2 monitor readings. A mixed venous blood sample was collected and analysed on a laboratory cooximeter. This confirmed an SvO_2 of 40%. Approximately ten minutes later there was a rapid decrease in SaO_2 to 65%. The patient was noted to be cyanotic and his PaO_2 was 39 mmHg (Table). Examination of the patient and ventilator circuit revealed adequate delivery of O_2 100% to both lungs, normal chest expansion and air entry bilaterally. A presumptive diagnosis of intrapulmonary shunting aggravated by SNP was made. The infusion of SNP was stopped. The ventilator settings were changed to increase minute ventilation from $7.0 \text{ litres}\cdot\text{min}^{-1}$ to $10.2 \text{ litres}\cdot\text{min}^{-1}$ and 10 cm H_2O of positive end expiratory pressure (PEEP) were added. A 100 mg bolus of amrinone was given followed by an infusion at $10 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$. The CI remained at $2.4\text{--}2.6 \text{ l}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$ in the next 30 min during which SaO_2 and SvO_2 increased to $>90\%$ and $>65\%$ respectively. There were no changes in ST segment in leads II or V_5 during this

TABLE Arterial blood gas and hematological results performed during the operative procedures.

	<i>Post-induction</i>	<i>Post Mitral Valve Repair</i>	<i>Post Mitral Valve Annuloplasty</i>	<i>Post Mitral Valve Replacement</i>	<i>During SNP Infusion</i>	<i>end of SNP Infusion</i>	<i>After SNP Infusion</i>	<i>Arrival to ICU</i>
<i>Time</i>	<i>08:40</i>	<i>11:35</i>	<i>14:15</i>	<i>16:45</i>	<i>17:45</i>	<i>18:05</i>	<i>18:25</i>	<i>19:15</i>
	A		B	C	D	E	F	
FiO ₂ (%)	100	100	100	100	100	100	100	80
pH	7.43	7.43	7.37	7.32	7.33	7.25	7.34	7.37
PaO ₂ (mmHg)	458	397	282	142	62	39	70	112
PaCO ₂ (mmHg)	36	30	38	44	44	57	43	38
SaO ₂ (%)	100	100	100	98	89	63	93	98
SvO ₂ (%)	85	70	70	65	50	39	60	65
A-a (mmHg)	210	279	384	516	596	603	589	411
a/A	0.69	0.59	0.42	0.22	0.09	0.06	0.11	0.21
Qs/Qt (%)	10	14	21	31	42	68	36	22
BE (mM·l ⁻¹)	0.3	-3.6	-2.4	-2.3	-1.7	-1.6	-1.7	-0.2
Hb (g·l ⁻¹)	133	83	77	73	70	87	100	100

Abbreviations: SNP, Sodium nitroprusside; ICU, Intensive Care Unit; A-a, Alveolar to arterial oxygen partial pressure gradient; a/A, arterial to Alveolar oxygen partial pressure ratio (Normal 0.85); Qs/Qt, Intrapulmonary shunt fraction; BE, Base Excess; Hb, Hemoglobin.

time. A prolonged three day period of postoperative ventilation was necessary as the patient required levels of PEEP up to 10 cm H₂O and high inspired concentrations of oxygen up to 100% to maintain adequate oxygenation. The patient subsequently recovered and was discharged home 15 days after his MVR.

Discussion

We believe that the profound hypoxemia observed in this case can be explained, in large part, by the interaction of SNP with three important factors that determine arterial oxygen saturation: intrapulmonary shunt, mixed venous blood desaturation, and intracardiac shunt.

Low cardiac output is common after valvular surgery. Conventional therapy utilizing an inotrope and a vasodilator offers the advantages of greater augmentation of cardiac output, better blood pressure control and improved organ perfusion compared with inotropic therapy alone¹ and SNP is one of the vasodilators advocated to improve CO after cardiac surgery.² Although SNP can increase cardiac output by reducing afterload, it can also increase intrapulmonary shunt due to inhibition of compensatory hypoxic pulmonary vasoconstriction (HPV).^{3,4}

This patient developed a severe shunt (Qs/Qt) intraoperatively (Table). The Qs/Qt reached a maximum of 68% as calculated from the shunt equation.⁵ The etiology of this shunt was multifactorial and probably involved the patient's preoperative pulmonary and cardiac status as well as events related to cardiac surgery itself. The patient's history and physical examination

suggested the presence of COPD with areas of ventilation/perfusion mismatch and compensatory HPV. The perioperative factors which may have led to increased intrapulmonary Qs/Qt included anesthesia,⁶ muscle relaxants^{6,7} and CPB.⁸ In retrospect, this complication might have been anticipated from the large A-a O₂ gradient or low a/A oxygen ratio (normal ≥ 0.85) that was present before starting the SNP infusion.

It is notable that the SvO₂ decreased ten minutes before the decrease in SaO₂ (Figure 1) despite an improved CO and increased hematocrit. The mechanism of this profound SvO₂ desaturation is unclear. Increased oxygen consumption due to subclinical shivering may be associated with increased CO and a large decrease of SvO₂.⁹ However, this is an unlikely explanation in this case because of the deep level of anesthesia and neuromuscular blockade at the time of the event. The fact that SvO₂ decreased shortly after SNP was started suggests that SNP induced venous desaturation before causing arterial hypoxemia. The administration of SNP may have caused vasodilatation and improved circulation in previously hypoperfused vascular beds, where considerable oxygen debt may have developed during the low CO state. If this occurred, blood with a very low oxygen content would have entered the venous circulation similar to what happens after cross-clamp removal during aortic surgery.¹⁰ This possible effect of SNP on venous blood oxygen content has not been described previously and remains speculative. One must also consider the possibility that the administration of SNP by lowering left atrial filling pressure

FIGURE 1 The changes in mixed venous oxygen saturation (SvO_2) and cardiac index (CI) following the termination of the third period of cardiopulmonary bypass are represented as seen on the Vigilance™ Monitor. Thick line = cardiac index. Thin line = mixed venous oxygen saturation. Sa = arterial oxygen saturation (pulse oximeter).

allowed right to left shunting of blood through the patent foramen ovale. Unfortunately we did not document this intraoperatively.

The relative contributions of decreasing SvO_2 and increasing Q_s/Q_t on arterial oxygen saturation can be determined by examining a plot of SvO_2 versus SaO_2 with isoshunt lines (Figure 2). Values were assigned to SvO_2 and Q_s/Q_t , and SaO_2 was calculated according to the formula in the Appendix. The isoshunt lines were then drawn by plotting SaO_2 against SvO_2 for each Q_s/Q_t , assuming FiO_2 is 1.0. The effect of SvO_2 on SaO_2 for a particular Q_s/Q_t may then be estimated or alternately the effect of Q_s/Q_t on SaO_2 may be estimated if SvO_2 is known. Figure 2 displays our patient's values at different times during the operation. Shunt increased from 10% at point (A) following induction of anesthesia to 31% at point (C) following the third separation from CPB but SaO_2 remained high because FiO_2 was 1.0 and SvO_2 was > 65% indicating adequate oxygen delivery. With the administration of SNP (D), Q_s/Q_t increased to 42% and at the same time SvO_2 decreased to 50% resulting in a decrease of SaO_2 to 89%. By the time SNP was discontinued at point (E), the combination of an increase in Q_s/Q_t to 68% with a decrease in SvO_2 to 39% resulted in profound arterial desaturation (SaO_2 = 63%, PaO_2 = 39 mmHg). Inspection of the diagram suggests that the increase in shunt alone would have brought the SaO_2 from 89% to 70%. The decrease in

FIGURE 2 The patient's values for mixed venous oxygen saturation (SvO_2) were plotted against arterial oxygen saturation (SaO_2) on a diagram indicating shunt fractions (Q_s/Q_t) represented as isoshunt lines (the thick diagonal lines labelled: 20, 40, 60, and 80%). Points A - F correspond to the clinical events listed in the table columns. The method used to calculate the points required to draw the figure is detailed in the Appendix. Because of the assumptions and approximations used in generating the diagram it is suitable only to the present discussion.

SvO_2 then further reduced the SaO_2 to 63%. The diagram is useful in illustrating the pathophysiology of hypoxemia. Similarly, it can be used to explain the improvement of SaO_2 after SNP was stopped and PEEP applied (F), when a large decrease in Q_s/Q_t and a large increase in SvO_2 were observed.

The continuous monitoring of CO and SvO_2 in this case gave an early warning of imbalance between oxygen delivery and consumption despite an improved CO and increased hematocrit following transfusion. If CO alone had been monitored the contribution of low SvO_2 to the arterial hypoxemia would not have been appreciated. Sampling of blood from the distal port (PA) of the PA catheter also allows assessment of SvO_2 but must be motivated by clinical suspicion.

In summary, the unusual arterial oxygen desaturation observed in this case was likely caused by right to left shunting of profoundly desaturated mixed venous blood via regions of the lung with low ventilation/perfusion ratio as well as via a patent foramen ovale. All three factors (intrapulmonary shunt, mixed venous desaturation, and intracardiac shunt) may have been exacerbated by treatment with SNP.

Appendix

Isoshunt lines defining the effect of SvO₂ on SaO₂ for different Qs/Qt

$$(1) Q_s/Q_t = (CcO_2 - CaO_2) / (CcO_2 - CvO_2)$$

INTRAPULMONARY SHUNT EQUATION

Where Q_s/Q_t = intrapulmonary shunt, CcO_2 = pulmonary end-capillary oxygen content, CaO_2 = arterial oxygen content, CvO_2 = mixed venous oxygen content. From (1) the following equation is derived:

$$(2) CaO_2 = CcO_2 - [Q_s/Q_t \times (CcO_2 - CvO_2)]$$

CcO_2 and CvO_2 may be calculated from the following equations

$$(3) CcO_2 = (S_{AO_2} \times 1.37 \times Hb) + (P_{AO_2} \times 0.003)$$

$$(4) CvO_2 = (SvO_2 \times 1.37 \times Hb) + (PvO_2 \times 0.003)$$

Where S_{AO_2} = oxygen saturation in the alveolus, P_{AO_2} = partial pressure of oxygen in the alveolus, SvO_2 = mixed venous blood oxygen saturation and PvO_2 = partial pressure of oxygen in mixed venous blood. SvO_2 is assigned values and PvO_2 is estimated from the oxyhemoglobin dissociation curve using these assigned SvO_2 values.¹¹ Assume pH = 7.4, Base excess = 0, temperature = 37°C.

P_{AO_2} may be calculated from

$$(5) P_{AO_2} = [FiO_2 \times (P_B - P_{H_2O}) - (PaCO_2/R)]$$

ALVEOLAR GAS EQUATION

P_B , barometric pressure is 760 mmHg and P_{H_2O} , water vapour pressure at body temperature is 47 mmHg. R , respiratory quotient is assumed to be 0.8.

Now, from the oxygen content formula

$$(6) CaO_2 = (SaO_2 \times 1.37 \times Hb) + (PaO_2 \times 0.003)$$

Whenever $PaO_2 < 100$ mmHg the contribution that dissolved oxygen makes to the total arterial oxygen content was ignored. This introduces an error of < 2.5% and the formula becomes:

$$(7) CaO_2 = SaO_2 \times 1.37 \times Hb \text{ and}$$

$$(8) SaO_2 = CaO_2 / (1.37 \times Hb)$$

Therefore utilizing equations (2) and (8) it is possible to calculate SaO_2 for different values of SvO_2 and Q_s/Q_t . SaO_2 is then plotted against SvO_2 for each Q_s/Q_t to generate Figure 2. Constants: $Hb = 10$ g·dl⁻¹, 1.37 ml of O₂ are carried by each 1g of fully saturated Hb, pH = 7.4, $PaCO_2 = 40$ mmHg, $FiO_2 = 1.0$.

References

- 1 Kaplan JA, Guffin AV. Treatment of perioperative left ventricular failure. In: Kaplan JA (Ed.). Cardiac Anesthesia, 3rd ed. Philadelphia, PA: WB Saunders Co., 1993: 1088-9.
- 2 Casthely PA, Lear S, Cottrell JE, Lear E. Intrapulmonary shunting during induced hypotension. Anesth Analg 1982; 61: 231-5.
- 3 D'Olivera M, Sykes MK, Chakrabarti MK, Orchard C, Keslin J. Depression of hypoxic pulmonary vasoconstriction by sodium nitroprusside and glyceryltrinitrate. Br J Anaesth 1981; 53: 11-7.
- 4 Bennumof JL. Hypoxic pulmonary vasoconstriction and infusion of sodium nitroprusside (Editorial). Anesthesiology 1979; 50: 481-3.
- 5 Nunn JF. Distribution of pulmonary ventilation and perfusion. In: Nunn JF (Ed.). Applied Respiratory Physiology, 3rd ed. Cambridge, UK: Butterworths, 1987: 140-83.
- 6 Hachenberg T, Tenling A, Nyström S-O, Tyden H, Hedenstierna G. Ventilation-perfusion inequality in patients undergoing cardiac surgery. Anesthesiology 1994; 80: 509-19.
- 7 Hedenstierna G, Tokics L, Strandberg A, Lundquist H, Brismar B. Correlation of gas exchange impairment to development of atelectasis during anesthesia and muscle paralysis. Acta Anaesthesiol Scand 1986; 30: 183-91.
- 8 MacNaughton PD, Braude S, Hunter DN, Denison DM, Evans TW. Changes in lung function and pulmonary capillary permeability after cardiopulmonary bypass. Crit Care Med 1992; 20: 1289-94.
- 9 Viale JP, Annat G, Lehot JJ, et al. Relationship between oxygen uptake and mixed venous oxygen saturation in the immediate postoperative period. Anesthesiology 1994; 80: 278-83.
- 10 Viale JP, Annat G, Ravat F, et al. Oxygen uptake and mixed venous oxygen saturation during aortic surgery and the first three postoperative hours. Anesth Analg 1991; 73: 530-5.
- 11 Kelman GR, Nunn JF. Nomograms for correction of blood PO₂, PCO₂, pH and base excess for time and temperature. J Appl Physiol 1966; 21: 1484-90.