Pulmonary gas exchange effects by nitroglycerin, dopamine and dobutamine during one-lung ventilation in man

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The effects of nitroglycerin, dopamine and dobutamine on pulmonary gas exchange were determined in 21 adult patients during two-lung and one-lung ventilation. Nitroglycerin, in 1 $\mu g \cdot kg^{-1} \cdot min^{-1}$, decreased cardiac index (CI) and PaO_2 during both two- and one-lung ventilation, and increased in $\dot{Q}s/\dot{Q}t$ during one-lung ventilation. There were no significant changes in the measured variables during infusion of dopamine, 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$. Dobutamine, 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$, increased CI and PaO_2 did not change during two-lung ventilation. During one-lung ventilation, PaO_2 increased from (mean value ± SD) 168 ± 46 to 201 ± 52 mmHg (P < 0.01) with dobutamine infusion. $\dot{Q}s/\dot{Q}t$ decreased from 29.2 ± 7.0 to 26.0 ± 6.2 per cent (P < 0.05) without any change in pulmonary vascular resistance index during one-lung ventilation. We conclude that dobutamine has advantages over dopamine and nitroglycerin during one-lung ventilation.

Dopamine and dobutamine are widely used as inotropic agents in patients with low cardiac output states.[1-4] Nitroglycerin is used as a vasodilator in patients with severe congestive heart failure. Such patients often have an acute or chronic lung disease with arterial hypoxaemia and may suffer a further decrease in arterial PaO_2 with these drugs.[5] In order to examine the action of these drugs under circumstances which are closer to the clinical situation, we studied their action on blood-gas exchange during two- and one-lung ventilation during surgery.

Methods

Following informed consent, we studied 21 adult patients, 15 men and six women, undergoing elective thoracotomy. Their age, mean ± SD, was 56 ± 5 years; weight, 58 ± 11 kg. Pulmonary function testing, performed preoperatively with the patients in the sitting position, included vital capacity (VC), forced vital capacity (FVC) and forced expiratory volume in one second (FEV1). No patient had cardiac disease. The study was described in detail to all subjects, and their consent was obtained.

All patients received premedication with 0.5 mg of atropine. Anaesthesia was induced with thiopentone and pancuronium and maintained with enflurane, N_2O and O_2, delivered through a Robertshaw double-lumen tube. The position of the bronchial tube was checked by inflating each lung separately while auscultating air entry. The absence of leaks was confirmed by ventilating one lung at a positive end–expiratory pressure of 20 cmH_2O and detecting any leak to the opposite lung by a balloon attached to the proximal end of the tube connection. The lungs of all patients were ventilated mechanically at 10–12 breaths $\cdot$ min^{-1} with a tidal volume of 12 ml $\cdot$ kg^{-1} (FIO_2 0.33).

In all patients, after induction of anaesthesia, a thermistor-tipped Swan-Ganz catheter (93A-1B-7A Edwards Laboratories) was inserted percutaneously via the right internal jugular vein. The catheter was floated into the wedge position and then withdrawn a few centimeters.

After ensuring steady-state conditions for 20 min with two-lung ventilation with the patient in the lateral position, haemodynamic and blood gas determinations were performed. Then 21 patients were randomly assigned to the three groups and received one of the following three drugs: nitroglycerin, 1 $\mu g \cdot kg^{-1} \cdot min^{-1}$ (n = 7); dopamine, 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ (n = 7); or dobutamine, 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ (n = 7). Measurements were done after 20 min of drug infusion which was then stopped, and the operation started.

After thoracotomy, one-lung ventilation was begun without alteration in tidal volume or rate. The FiO_2 was set to maintain the PaO_2 at approximately 90 mmHg.

The control measurements during one-lung ventilation were obtained 20 minutes after collapse of the non-dependent lung. Drug infusion was started again and after 20 min measurements were repeated. All measurements were completed before either occlusion or division of the pulmonary artery.

Measurements consisted of systemic arterial (AP), pulmonary artery (PAP), pulmonary capillary wedge (PCWP) and airway (Paw) pressures, and cardiac outputs (CO). Cardiac output was determined by thermodilution. The thermal indicator was 10 ml of five per cent glucose at 0–2° C, injected into the right atrium. Cardiac output was derived from the mean of three consecutive measurements.

Blood gas tensions and pH of arterial and mixed venous blood were measured using a Corning 178 blood-gas analyzer and were corrected to the patient's temperature.

Physiological shunt ($\dot{Q}s/\dot{Q}t$) was calculated using standard equations.*

Data were expressed as mean ± SD. Statistical analyses were performed using Student's t test and the level of significance was defined as P < 0.05.

Results

Mean data for preoperative pulmonary function are listed in Table I.

Haemodynamic values are shown in Table II. During two-lung ventilation, nitroglycerin produced significant reduction in cardiac index (CI), mean aortic pressure (MAP) and PaO_2 and a significant increase in heart rate (HR).

With one-lung ventilation, nitroglycerin produced significant reduction in MAP, CI, mean pulmonary artery pressure (MPAP) and PaO_2, and a significant increase in $\dot{Q}s/\dot{Q}t$. With two-lung ventilation, PaO_2 decreased by 8

*$\dot{Q}s/\dot{Q}t = (C\acute{c}O_2 - CaO_2)/(C\acute{c}O_2 - C\bar{v}O_2) \times 100$
$C\acute{c}O_2 = Hb \times 1.39 \pm 0.003 \times PAO_2$
(respiratory quotient 0.8).

TABLE I   Preoperative pulmonary function

	Nitroglycerin n = 7	Dopamine n = 7	Dobutamine n = 7
VC (%)	98 ± 12	94 ± 21	101 ± 12
FVC1% (%)	83 ± 8	70 ± 8	72 ± 10
FEV1 (L)	2.6 ± 0.4	2.0 ± 0.5	2.3 ± 0.6

Values are mean ± SD.

mmHg (P < 0.05) and with one-lung ventilation, PaO_2 decreased by 42 mmHg (P < 0.01) (Table III).

There were no significant changes in any of the measured variables during dopamine administration.

Dobutamine, administered during two-lung ventilation, increased HR and CI, while $\dot{Q}s/\dot{Q}t$ and PaO_2 were not changed. During one-lung ventilation, dobutamine increased HR, CI, MPAP and PaO_2, and decreased $\dot{Q}s/\dot{Q}t$. With two-lung ventilation, PaO_2 did not change, but with one-lung ventilation, PaO_2 increased by 33 mmHg (P < 0.01). $\dot{Q}s/\dot{Q}t$ did not change with two-lung ventilation, but with one-lung ventilation, $\dot{Q}s/\dot{Q}t$ decreased by 3.2 per cent (P < 0.05) (Table IV).

Discussion

We wished to determine the effects of nitroglycerin, dopamine and dobutamine infusion on blood-gas exchange during one-lung ventilation. We found that nitroglycerin, administered during one-lung ventilation, decreased PaO_2 and increased $\dot{Q}s/\dot{Q}t$. During two-lung ventilation, the effect of nitroglycerin on gas exchange was similar in direction but less in magnitude. This suggests that nitroglycerin impaired pulmonary gas exchange in the presence of one-lung ventilation.

Induction of hypoxic pulmonary vasoconstriction (HPV) was first demonstrated by Von Euler and Liljestrand.[6] Later, HPV was found to occur in all mammalian species tested, including man.[7,8] The teleologic purpose of HPV is to drive blood from hypoxic alveoli and thereby to improve ventilation: perfusion relationships.[6-9] Much speculation has been raised concerning the pharmacological inhibition of HPV by anaesthetic agents and vasodilators in experiments performed on laboratory animals.[10-12]

Fahmy[13] showed that intravenous nitroglycerin was associated with a reduction in PaO_2 in anaesthetized patients. Hales et al.[14] have found, that by ventilating dog lungs with nitrogen, nitroglycerin inhibits HPV. Also, Mookherjee et al.[15] showed that sublingual nitroglycerin caused a small but significant increase in venous admixture of 3.8 per cent in patients being evaluated for chest pain. Therefore, it is likely that nitroglycerin impairs pulmonary gas exchange by inhibiting HPV, resulting in

TABLE II   Effects of nitroglycerin on various haemodynamic and blood gas variables during two- and one-lung ventilation

Stage	A Two-lung FIO_2 0.33 baseline	B Two-lung FIO_2 0.33 1 µg·kg^{-1}·min^{-1}	C One-lung FIO_2 0.5–1 baseline	D One-lung FIO_2 0.5–1 1 µg·kg^{-1}·min^{-1}
HR (beats·min^{-1})	91 ± 7	103 ± 8*	98 ± 3	100 ± 8
MAP (mmHg)	89 ± 7	75 ± 6*	99 ± 9	83 ± 14*
CI (1·min^{-1}·m^{-2})	3.3 ± 0.6	2.9 ± 0.5*	3.4 ± 0.6	2.9 ± 0.7*
MPAP (mmHg)	15 ± 3	13 ± 3	19 ± 4	17 ± 3*
PCWP (mmHg)	7.1 ± 1.2	6.6 ± 1.4	10 ± 2.7	9.8 ± 2.8
PVRI (dyne·s·cm^{-5}·m^{-2})	191 ± 52	176 ± 35	212 ± 82	198 ± 64
Qs/Qt (%)	9.2 ± 3.0	10.8 ± 3.4	29.2 ± 4.9	34.6 ± 5.0†
pH	7.40 ± 0.05	7.37 ± 0.06	7.39 ± 0.04	7.41 ± 0.06
PaCO_2 (mmHg)	37 ± 6	39 ± 4	38 ± 5	38 ± 6
PaO_2 (mmHg)	137 ± 22	129 ± 24*	186 ± 30	144 ± 29†
Paw (cmH_2O)	17 ± 2	17 ± 3	22 ± 2	22 ± 3

Values are mean ± SD.
*P < 0.05.
†P < 0.01.

TABLE III   Effects of dopamine on various haemodynamic and blood gas variables during two- and one-lung ventilation

Stage	A Two-lung FIO_2 0.33 baseline	B Two-lung FIO_2 0.33 5 µg·kg^{-1}·min^{-1}	C One-lung FIO_2 0.5–1 baseline	D One-lung FIO_2 0.5–1 5 µg·kg^{-1}·min^{-1}
HR (beats·min^{-1})	73 ± 9	85 ± 7	94 ± 12	91 ± 10
MAP (mmHg)	85 ± 12	91 ± 11	76 ± 12	81 ± 15
CI (1·min^{-1}·m^{-2})	3.1 ± 0.5	3.2 ± 0.4	3.4 ± 0.6	3.5 ± 0.7
MPAP (mmHg)	14 ± 2	15 ± 3	17 ± 3	19 ±4
PCWP (mmHg)	6.9 ± 1.8	6.4 ± 1.5	7.3 ± 2.5	8.3 ± 2.6
PVRI (dyne·s·cm^{-5}·m^{-2})	183 ± 75	215 ± 59	228 ± 62	244 ± 54
Qs/Qt (%)	8.1 ± 0.9	9.0 ± 2.4	30.7 ± 5.5	27.8 ± 4.8
pH	7.40 ± 0.04	7.39 ± 0.05	7.37 ± 0.05	7.37 ± 0.05
PaCO_2 (mmHg)	35 ± 2	35 ± 6	36 ± 3	37 ± 2
PaO_2 (mmHg)	131 ± 15	121 ± 12	163 ± 40	179 ± 37
Paw (cmH_2O)	16 ± 3	16 ± 2	23 ± 3	23 ± 3

Values are mean ± SD.
*P < 0.05.
†P < 0.01.

increased flow to poorly ventilated or unventilated regions of the lung.

Dopamine and dobutamine are currently used as inotropic agents in patients with circulatory and respiratory failure. Although there is agreement about their effects on the systemic circulation and cardiac function,[16,17] their effects on the pulmonary circulation remain controversial.

Both dopamine and dobutamine have been reported to not affect,[18-21] increase,[22] or decrease[5,23-25] normoxic pulmonary vascular tone. Hypoxic pulmonary vasoconstriction (HPV) was either unchanged,[26,27] enhanced,[28] or inhibited[29] after dopamine and inhibited[26,27] after dobutamine.

In our study, dobutamine administered during one-lung ventilation increased PaO_2 and decreased Qs/Qt. The ventilatory manoeuvres in these cases increased the volume of the ventilated dependent lung and influenced the intra-alveolar pressure. The distribution of blood between the ventilated and nonventilated lung can be influenced by the intra-alveolar pressure. Increased intra-

TABLE IV   Effects of dobutamine on various haemodynamic and blood gas variables during two- and one-lung ventilation

Stage	A Two-lung FIO_2 0.33 baseline	B Two-lung FIO_2 0.33 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$	C One-lung FIO_2 0.5–1 baseline	D One-lung FIO_2 0.5–1 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$
HR (beats · min^{-1})	87 ± 10	104 ± 6*	99 ± 8	109 ± 12*
MAP (mmHg)	84 ± 8	92 ± 8	87 ± 15	95 ± 9
CI (l · $min^{-1} \cdot m^{-2}$)	3.0 ± 0.6	3.5 ± 0.5*	3.3 ± 0.3	4.1 ± 0.4*
MPAP (mmHg)	14 ± 3	14 ± 2	18 ± 3	21 ± 3*
PCWP (mmHg)	7.6 ± 1.2	7.4 ± 2.5	9.1 ± 2.4	10 ± 2.5
PVRI (dyne · s · $cm^{-5} \cdot m^{-2}$)	170 ± 45	151 ± 52	215 ± 68	212 ± 55
Qs/Qt (%)	10.6 ± 3.4	11.7 ± 2.8	29.2 ± 7.0	26.0 ± 6.2*
pH	7.37 ± 0.04	7.35 ± 0.03	7.39 ± 0.03	7.38 ± 0.04
$PaCO_2$ (mmHg)	38 ± 4	39 ± 5	37 ± 3	38 ± 3
PaO_2 (mmHg)	129 ± 18	125 ± 19	168 ± 46	201 ± 52†
Paw (cmH$_2$O)	16 ± 2	16 ± 2	23 ± 2	22 ± 3

Values are mean ± SD.
*P < 0.05.
†P < 0.01.

alveolar pressure can increase pulmonary vascular resistance in ventilated areas and thereby reapportion ventilated and nonventilated lung. The Qs/Qt would ultimately be determined by the balance between dependent lung recruitment and increased vascular resistance in that lung. In these conditions, dobutamine infused in clinical doses increased cardiac output. The explanation for the improvement in PaO_2 and Qs/Qt is probably an increase of pulmonary blood flow to the dependent lung.

It is concluded that dobutamine has advantages over dopamine during one-lung ventilation. Nitroglycerin can cause a marked decrease in PaO_2 and an increase in Qs/Qt during one-lung ventilation. Thus, nitroglycerin is capable of adversely affecting pulmonary gas exchange which may lead to a decrease in PaO_2.

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Résumé

Les auteurs ont mesuré chez 21 adultes, l'effet de la nitroglycérine, de la dopamine ou de la dobutamine sur les échanges gazeux en ventilation uni- et bi-pulmonaire. A la dose de 1 $\mu g \cdot kg^{-1} \cdot min^{-1}$ la nitroglycérine diminuait l'index cardiaque (CI) et la PaO_2 tant en ventilation bi-qu'uni-pulmonaire alors qu'elle augmentait le $\dot{Q}s/\dot{Q}t$ de ce dernier mode. Ces mêmes variables sont demeurées inchangées par l'infusion de 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ de dopamine. La dobutamine, à raison de 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ ne modifia pas le CI ni la PaO_2 en ventilation bi-pulmonaire quoique avec elle, quand un seul poumon était ventilé, la PaO_2 passait de 168 ± 46 à 201 ± 52 mmHg (P < 0.01) et le $\dot{Q}s/\dot{Q}t$ de 29.2 ± 0.7 à 26.0 ± 6.2 (P < 0.05) et ce, sans changement de l'index de résistance vasculaire pulmonaire. La supériorité de la dobutamine en ventilation uni-pulmonaire est ainsi établie.