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Original Papers

The Effects on Increasing Cardiac Output with Adrenaline or Isoprenaline on Arterial Haemoglobin Oxygen Saturation and Shunt During One-Lung Ventilation

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SUMMARY

Theoretically, if the cardiac output were increased in the presence of a given intrapulmonary shunt, the arterial haemoglobin oxygen saturation (SaO_2) should improve as the venous oxygen extraction per ml of blood decreases. To test this hypothesis, eight pigs were subjected to one-lung ventilation and adrenaline and isoprenaline infusions used to increase the cardiac output. The mixed venous oxygen, shunt fraction and oxygen consumption were measured.

With both adrenaline and isoprenaline, although there was a small rise in mixed venous oxygen content, there was a fall in SaO_2. With adrenaline, the mean shunt rose from 48% to 65%, the mean oxygen consumption rose from 126 ml/min to 134 ml/min and the mean SaO_2 fell from 86.9% to 82.5%. With isoprenaline, the mean shunt rose from 45% to 59%, the mean oxygen consumption rose from 121 ml/min to 137 ml/min and the mean SaO_2 fell from 89.5% to 84.7%.

It is concluded that potential improvement in SaO_2, which might occur from a catecholamine-induced increase in mixed venous oxygen content during one-lung ventilation, is more than offset by increased shunting and oxygen consumption which reduce SaO_2.

Key Words: VENTILATION: one-lung, hypoxia; HEART: cardiac output, adrenaline, isoprenaline

One-lung ventilation is commonly used for intrathoracic procedures. Occasionally, in spite of an optimal position of the double-lumen tube, major decreases in SaO_2 occur. With 100% inspired oxygen and a given oxygen consumption, the degree of desaturation is dependant on only two factors, the shunt fraction and the level of desaturation in the mixed venous blood. For a given shunt fraction, the SaO_2 will rise as the mixed venous oxygen content rises. Thus one possible approach to minimizing the decrease in SaO_2 would be to elevate the mixed venous oxygen content.

The oxygen content of mixed venous blood is determined by the initial level of arterial oxygen content, the tissue oxygen uptake and the cardiac output. If the oxygen tissue uptake (oxygen consumption) remains unaltered, increasing the cardiac output should result in a higher mixed venous oxygen content and a better arterial oxygen saturation as a consequence. Thus the SaO_2 during one-lung anaesthesia should improve if the cardiac output could be increased without increasing the shunt fraction or the oxygen uptake. To test this hypothesis we stimulated the cardiac output with adrenaline or isoprenaline in pigs who were being ventilated using one-lung under general anaesthesia.

METHODS

This study was approved in advance by the animal ethics committee of the University of Cape Town.

Pigs weighing between 23 and 25 kg were premedicated intramuscularly with ketamine 300 mg, diazepam 2.5 mg and atropine 0.6 mg. After the pig was very drowsy, a cannula was inserted into an ear vein and thiopentone administered intravenously until the animal was unconscious. The pig was then intubated with a 7.0 mm cuffed tracheal tube, pancuronium 8 mg administered and the lungs ventilated

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with oxygen and 1% halothane. Arterial cannulation was established by a cut-down into the right carotid artery. A pulmonary artery catheter was placed via the right external or internal jugular vein. Halothane administration was varied between 0.5% and 2% as determined by the arterial blood pressure and heart rate. Additional pancuronium 2 mg and ketamine 100 mg were administered every half hour to maintain haemodynamic stability and to ensure an adequate depth of anaesthesia. Nasopharyngeal temperature was monitored and the temperature maintained between 35.5 and 37.5°C with hot air warming. Heart rate (ECG) and blood pressure were monitored continuously and recorded every minute directly from the monitor into a computer.

Once monitoring had been established, a tracheostomy was made and the tracheal tube replaced by a 35 Fr left-sided double-lumen endobronchial tube through the tracheostomy. The bronchial cuff was inflated to achieve a seal in the trachea. The lung inflation pressure was noted (usually about 25 cmH_2O) and with the cuff inflated, the tube advanced about 1cm with each breath. Placement of the tube in the left main bronchus was evidenced by a firm resistance to further advancement, a fall in lung compliance (as seen by a sharp rise in inflation pressure for the set tidal volume), asymmetry of chest movement and breath sounds and a sharp fall in SaO_2. Once this was achieved, the cuff was deflated and the tube moved in a further 15 mm. The tube was then sutured to the skin to reduce further movement.

Ventilation was adjusted to achieve a P_aCO_2 between 30 and 45 mmHg. Cardiac output was measured in triplicate by cold thermodilution. Duplicate arterial and mixed venous samples for analysis of PO_2, haemoglobin oxygen saturation and PCO_2 were taken and the cardiac output again measured in triplicate. Haemoglobin concentration was measured. The shunt fraction was calculated with the standard equations using an alveolar oxygen pressure of 100% less water vapour and arterial CO_2 tension. Oxygen consumption was calculated as the difference between the arterial and venous oxygen content multiplied by the averaged pre-sample and post-sample cardiac outputs.

Cardiac output was then stimulated by an intravenous infusion of adrenaline or isoprenaline. The initial infusion for adrenaline was 1 $\mu g.min^{-1}$ and for isoprenaline was 0.2 $\mu g.min^{-1}$. The first drug used on each pair of pigs was selected randomly by the toss of a coin; the second pig of the pair received the opposite sequence of sympathomimetic drugs.

The rate of drug infusion was increased every two minutes. The aim was to achieve at least a 30% increase in cardiac output. Once a satisfactory increase in cardiac output had been achieved, the infusion was maintained for 10 minutes and a triplicate set of cardiac output measurements taken. This was followed by arterial and mixed venous blood samples taken in duplicate and finally a further set of triplicate cardiac output measurements.

The sympathomimetic infusion was then ceased and the heart rate and cardiac output allowed to settle usually within ±10% of the previous values. After 15 minutes the cardiac output and blood gases were again measured. The second infusion was then commenced to the same target increase in cardiac output. Once the values had been stable for 10 minutes, cardiac output and blood gases were measured. The infusion was stopped and after a further 15 minutes the measurements repeated. Changes in output and other parameters were measured against the average value of the preceding and following control states.

At the end of the experiment the pig was killed with an overdose of thiopentone and intravenous air. The bronchial tree and lungs were subjected to a post mortem examination to ensure that ventilation of only the left lung had been achieved. At this time, the presence and position of an upper lobe bronchus supplying either lung arising directly from the trachea was also examined.

Statistical analysis was done using Statview 5.0 (SAS) and Instat 2. For most comparisons, a paired t test was used. For all probabilities, a two-tailed test was used. In the results, mean values are given with standard deviations.

RESULTS

The experimental protocol was completed in eight pigs. All pigs had a direct bronchial airway from the trachea to the right upper lobe. In all animals, the final intubation had excluded the right lung. In seven of the eight pigs, the intubation had excluded also the bronchial branch to the left upper lobe.

Cardiac Outputs

The control cardiac outputs ranged from 2.3 to 4.3 l/min. The percentage increase in cardiac output with adrenaline ranged from 54% to 87% and with isoprenaline from 31% to 110%.

Mixed Venous Oxygen Contents

Mixed venous oxygen content rose with all adrenaline and isoprenaline infusions. The mean increase

with adrenaline was 1.66±1.03 ml%, range 0.42 to 3.34 (P=0.003). The mean increase with isoprenaline was 0.64±0.43 ml% range 0.04 to 1.134 (P=0.004).

Arterial Haemoglobin Oxygen Saturation

The control SaO_2 varied from 69.0% to 99.6%, with a mean of 86.9±7.9%. During adrenaline infusion, the mean SaO_2 varied from 64.5% to 96% with a mean of 82.5±10.6%. The mean change in SaO_2 was =4.4±3.5%, t=3.54, P=0.0094. The control SaO_2 for isoprenaline varied from 80.9% to 100%, with a mean of 89.5±5.8%. During isoprenaline infusion, the SaO_2 varied from 68.8% to 96.4% with a mean of 84.7±7.7%. The mean change in SaO_2 was 4.8± 3.6%, t=3.76, P=0.0071.

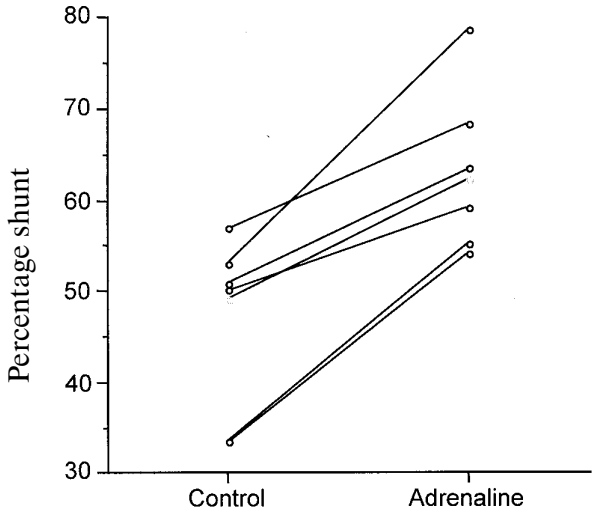

FIGURE 1: The effect of adrenaline infusion on the shunt. In all pigs the shunt increased; the mean (SD) increase was 16.8±5.9%, t=8.1, P<0.0001.

Shunt

For the whole group, the control shunt was 48.1±6.9%. After the administration of adrenaline, the shunt increased to 64.9±7.8%. The mean difference between control shunt and the shunt during adrenaline infusion was 16.8±5.9% (paired t=8.1, P<0.0001) (Figure 1).

The control shunt prior to the administration of isoprenaline was 44.9±7.4% which is not significantly different from the adrenaline control (P=0.39). During the isoprenaline infusion, the mean shunt increased to 59.3±3.7% which was again not significantly different from the shunt during the adrenaline infusion, but was significantly greater than the control shunt. The mean difference in shunt from control for the isoprenaline infusions was 14.3±4.7% (paired t=8.6, P<0.0001) (Figure 2).

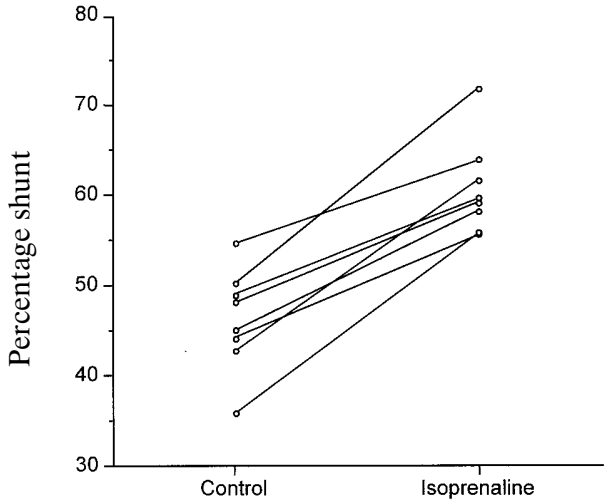

FIGURE 2: The effect of isoprenaline infusion on the shunt. In all pigs the shunt increased; the mean (SD) increase was 14.3+4.7%, t=8.6, P<0.0001.

Oxygen Consumption

For the whole group, the mean control oxygen consumption was 126.2±30.2 ml/min. After the administration of adrenaline, the mean consumption increased to 133.8±43.7 ml/min. The mean difference between control and the oxygen consumption during adrenaline infusion was 7.7±25.6 ml/min (paired t=0.85, P=0.42) (Figure 3).

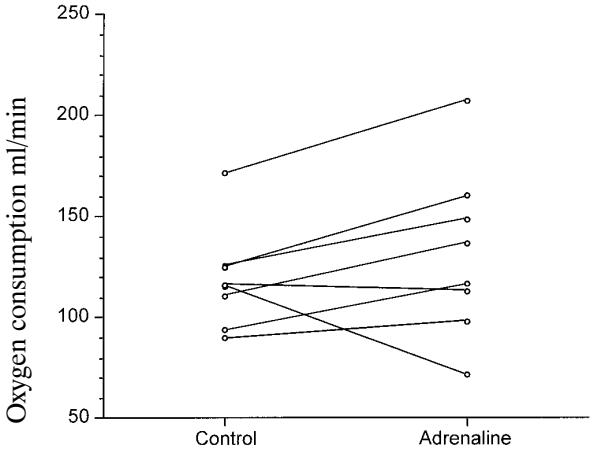

FIGURE 3: Change in oxygen consumption with an adrenaline infusion. Although there is a tendency to increase consumption; mean (SD) change 7.7±25.6 ml/min, the change is not statistically significant, t=0.85, P=0.42

Similarly during the administration of isoprenaline, oxygen consumption increased from the control value of 120.5±15.9 ml/min to 137.0±26.6 ml/min with a mean individual change of 16.6±18.4 ml/min, (paired t=2.6, P=0.038) (Figure 4). The control pre- and

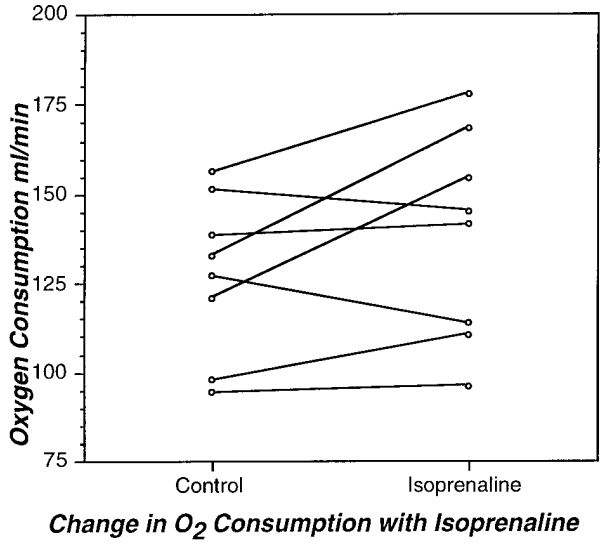

FIGURE 4: Changes in oxygen consumption with the infusion of isoprenaline. Overall, there was an increase in oxygen consumption; mean (SD), 16.6±18.4 ml/min, t=2.6, P=0.038.

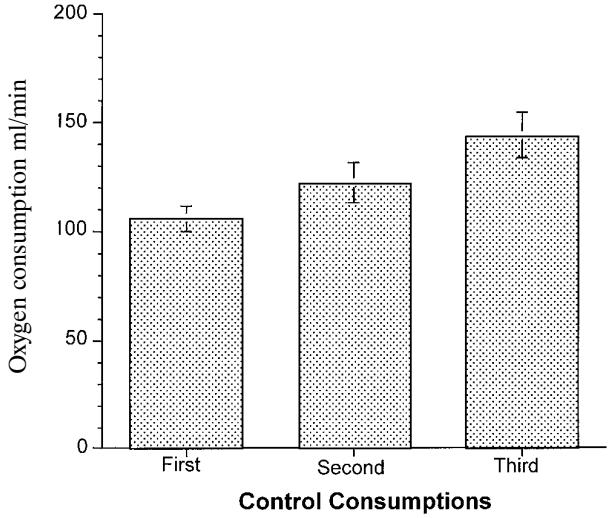

FIGURE 6: Percentage oxygen consumption and standard deviation for the eight pigs at each of the three control periods. There is a significant difference with respect to time. (One way ANOVA F=4.3, P=0.027.)

post-isoprenaline values for oxygen consumption were not significantly different from those pre- and post-adrenaline.

Other Changes

Three control measurements of shunt and oxygen consumption were made on each animal; an initial measurement was made before the first infusion and then two further measurements, one after each infusion. These control measurements of shunt were not significantly different between each of the three times (one-way ANOVA F=0.16, P=0.85) (Figure 5).

However, the oxygen consumption at the control intervals showed a progressive increase during the experiment (one-way ANOVA F=4.3, P=0.027) (Figure 6).

The increases in shunt and in oxygen consumption that accompanied the administration of adrenaline and of isoprenaline were individually only weakly correlated with the increase in cardiac output which occurred. However, the effect was more apparent when the two catecholamines were combined, both for shunt and for oxygen consumption (Figure 7 and Figure 8 respectively).

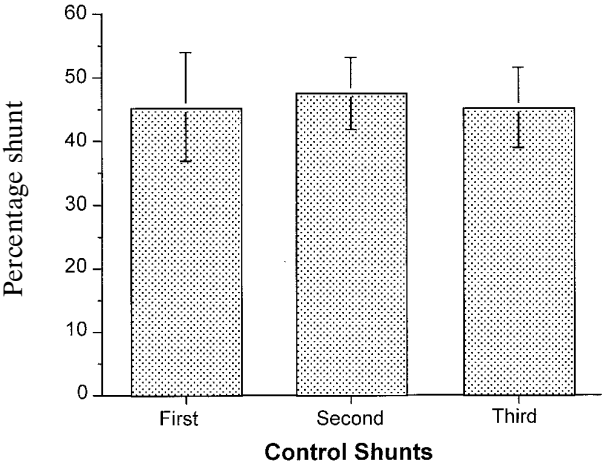

FIGURE 5: Percentage shunt and standard deviation for the eight pigs at each of the three control periods. There is no significant difference with respect to time (one-way ANOVA F=0.16, P=0.85).

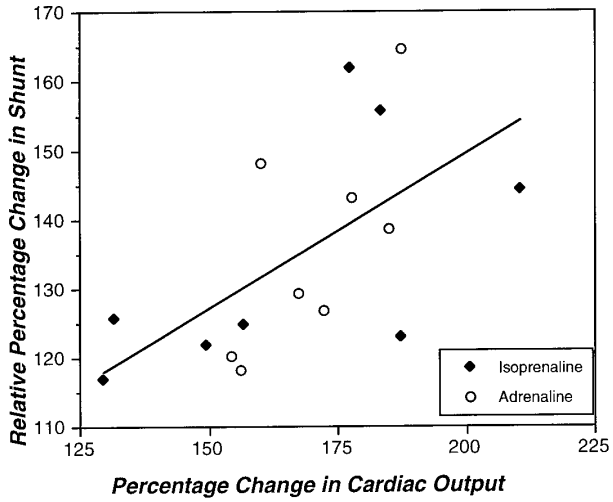

FIGURE 7: Relationship between cardiac output (x) and shunt (y). The regression equation is: y=0.45x –40.0 r=0.61, P=0.013.

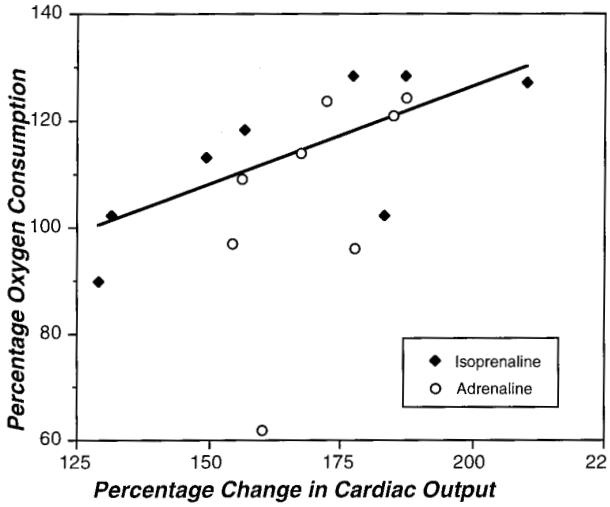

FIGURE 8: Relationship between cardiac output (x) and oxygen consumption (y). The regression equation is: y=0.43x+37.3 r=0.52, *P*=0.039.

DISCUSSION

In contrast to the study by Mouton et al[1] where the apical bronchus arising from the trachea was equally distributed between the right and left sides, the eight pigs in these experiments all had the right apical bronchus arising from the trachea. This simplified the protocol in that when the double-lumen tube was inserted into the left main bronchus for left lung ventilation, the right apical bronchus was excluded from ventilation with the rest of the right lung.

It is clear that in this pig model, in spite of an improved mixed venous oxygen, the use of either adrenaline or isoprenaline to boost cardiac output is associated with a significant decrease in SaO_2, in direct contradiction to the original hypothesis. This result is attributable to the effects of sympathomimetic stimulation on intrapulmonary shunting and oxygen consumption. The increased shunt could be the result of either inhibition of hypoxic vasoconstriction or direct intrapulmonary vasodilatation. Studies by Furman et al[2] and Marin[3] have shown that isoprenaline and dobutamine have pulmonary vasodilator properties that may inhibit hypoxic pulmonary vasoconstriction, although this has not been tested in a model with an atelectatic lung. It has also been suggested that vasoconstrictor drugs such as phenylephrine may preferentially constrict vessels in normoxic lung, thus increasing the flow through the hypoxic areas[4]. Our data cannot distinguish the effects of increased oxygen consumption and vasodilation increasing the shunt, but the net result is further desaturation of the arterial blood. Increased oxygen consumption reduces the rise in mixed venous oxygen expected with increased cardiac output. These effects outweigh the potential benefit of increased cardiac output increasing oxygen delivery to the tissues. The small rise in mixed venous oxygen content could indicate improved tissue oxygen delivery but may also be due to increased capillary shunting and reduced tissue oxygen delivery. Only direct tissue oxygen tension measurement could resolve these possibilities.

Although cardiac stimulants other than adrenaline and isoprenaline may be able to increase the cardiac output without adverse effects, the present evidence suggests that most potent inotropes do increase oxygen consumption[5]. Of the presently available inotropic agents, only dopamine appears not to increase oxygen consumption and thus may be of benefit[6], although there are no direct data that we are aware of to support this possibility. Whether other inotropic agents would produce similar increases in intrapulmonary shunting is uncertain, but it seems likely that any agent with significant beta-adrenergic activity would be likely to cause a similar degree of pulmonary vasodilation.

Although the 15 minute control periods were adequate to restore normal haemodynamic function and to reverse the adverse effects of intrapulmonary shunting, there was a progressive increase in oxygen consumption throughout the experiment. This increase in metabolic rate may be produced by a catecholamine effect which significantly outlasts the haemodynamic effects. It is possible that a longer control period between catecholamine infusions may have allowed more complete reversal of the metabolic effects. We could find no reported data on the duration of the metabolic effects of catecholamines in an intact animal model.

The correlation between the increase in cardiac output and both the increased shunt and the increased oxygen consumption for either type of catecholamine stimulation suggests that increasing cardiac output by the use of catecholamines will inevitably be offset by increases in oxygen consumption and in shunt. The results of this study strongly suggest that any attempt to improve SaO_2 during one-lung anaesthesia by stimulation of cardiac output with catecholamines is unlikely to be beneficial. The value of catecholamines with a greater vasoconstrictor effect remains to be investigated.

In conclusion, although enhancing the cardiac output with a catecholamine infusion might theoretically improve the SaO_2 for a given fixed shunt during one-lung anaesthesia, these experiments in pigs do not

support this hypothesis. An infusion of either adrenaline or isoprenaline is associated with an increased shunt and an increased oxygen consumption. These two effects more than offset any beneficial effect of an improved cardiac output on SaO_2..

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REFERENCES

1. Mouton WG, Pfitzner J, Bessel JR, Maddern GJ. Bronchial anatomy and single lung ventilation in the pig. Can J Anesth 1999; 46:701-703.
2. Furman WR, Summer WR, Kennedy TP, Sylvester JT. Comparison of the effects of dobutamine, dopamine and isoproterenol on hypoxic pulmonary vasoconstriction in the pig. Crit Care Med 1982; 10:371-374.
3. Marin JL, Orchard C, Chakrabarti MK, Sykes MK. Depression of hypoxic pulmonary vasoconstriction in the dog by dopamine and isoprenaline. Br J Anaesth 1979; 51:303-312
4. Doering EB, Hanson CW, Reily DJ, Marshall C, Marshall BE. Improvement in oxygenation by phenylephrine and nitric oxide in patients with adult respiratory distress syndrome. Anesthesiology 1997; 87:18-25.
5. Kazai W, Lötte A, Günnicker M, Vorgrimler-Karzai UM, Preibe H-J. Dopamine increases oxygen consumption during constant flow cardiopulmonary bypass. Br J Anaesth 1996; 76:5-8.
6. Kazai W, Günnicker M, Scharbert G, Vorgrimler-Karzai UM, Preibe H-J. Effects of dopamine on oxygen consumption and gastric mucosal blood flow during cardiopulmonary bypass in

humans. Br J Anaesth 1996; 77:603-606.