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# The Effects on Arterial Haemoglobin Oxygen Saturation and on Shunt of Increasing Cardiac Output with Dopamine or Dobutamine 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 saturation should improve as the venous oxygen extraction per ml of blood decreases if the total oxygen consumption remains constant. Previous work demonstrated that this was not achieved with adrenaline or isoprenaline as increased shunting negated any benefit from improved cardiac output and mixed venous oxygen content. However, pharmacological stimulation of cardiac output and venous oxygen without any increase in shunt should achieve the goal of improved arterial oxygenation. To test this hypothesis, seven pigs were subjected to one-lung ventilation and infused on separate occasions, with dopamine and with dobutamine in random order to increase the cardiac output. The mixed venous oxygen content, shunt fraction, oxygen consumption and arterial oxygen saturation were measured.*

*With both dopamine and dobutamine there was a consistent rise in venous oxygen content. However, with dopamine, the mean shunt rose from 28% to 42% and with dobutamine, the mean shunt rose from 45% to 59% (both changes $P<0.01$). With dopamine, the mean arterial oxygen saturation fell by 4.7%, and with dobutamine by 2.9%, but neither fall was statistically significant.*

*It is concluded that any benefit to arterial saturation which might occur from a dopamine- or dobutamine-induced increase in mixed venous oxygen content during one-lung ventilation is offset by increased shunting. During one-lung anaesthesia, there would appear to be no benefit to arterial saturation in increasing cardiac output with an infusion of either dopamine or dobutamine.*

Key Words: LUNG: shunting. VENTILATION: one-lung. HEART: dopamine, dobutamine, cardiac output. OXYGEN: saturation

The use of one-lung ventilation for many intrathoracic procedures is common. Occasionally, in spite of an optimal position of the double-lumen tube, major arterial desaturation occurs. With 100% inspired oxygen and a given oxygen consumption, the degree of arterial desaturation is dependent on only two factors, the shunt fraction and oxygen content of the mixed venous blood. For a given shunt fraction, the saturation in the arterial blood will rise as the mixed venous oxygen content rises. Thus one possible approach to minimizing the impact on the arterial saturation could be to elevate the mixed venous oxygen content as high as possible.

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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, if the shunt remains constant, a better arterial oxygen saturation as a secondary consequence. Thus the arterial saturation during one-lung anaesthesia should improve if the cardiac output were increased without increasing the shunt fraction. Previous attempts to do this by increasing the cardiac output with either adrenaline or isoprenaline failed to improve the arterial saturation, mainly because there was an increased shunt fraction in parallel with the rise in cardiac output, together with an increase in metabolic rate[1]. However, increasing cardiac output without altering the shunt fraction or peripheral oxygen consumption should be beneficial if the correct agent were found. To further test this hypothesis we stimulated the cardiac output with dopamine or

dobutamine in pigs who were being ventilated on one lung under general anaesthesia.

## METHODS

The animal ethics committee of the University of Cape Town approved this study in advance. Pigs weighing between 23 and 29 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's trachea was then intubated with a 7.0 mm cuffed tracheal tube. Once ventilation was established, pancuronium 8 mg was administered and the lungs ventilated with oxygen and 1% halothane. Arterial cannulation was established by a cut-down into the right carotid artery. After carotid artery cannulation, a pulmonary artery catheter was floated into position 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 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.

Once monitoring had been established, a tracheostomy was made and the tracheal tube was 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 1 cm 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 of breath sounds and a sharp fall in arterial oxygen saturation. 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. Once this was done, cardiac output was measured in triplicate by cold thermodilution. Duplicate arterial and mixed venous samples for analysis of $PO_2$, oxygen saturation and $PCO_2$ were taken and measured on a Radiometer ABL505 blood gas analyser. After these samples, the cardiac output was again measured in triplicate. With the measurement of blood gases, the haemoglobin content of each of the samples was also determined. The shunt fraction was calculated with the standard equations using an estimated alveolar oxygen pressure of 760 mmHg less water vapour and arterial $CO_2$ tension i.e. alveolar $PO_2 = 713 - P_aCO_2$, and alveolar capillary oxygen content was calculated as 1.34 ml x Hb (g/100 ml) + 0.003 ml x alveolar $PO_2$ (mmHg). 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 increased by an intravenous infusion of dopamine or dobutamine. 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 adjusted every two minutes. The aim was to achieve at least a 40% 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 was 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 control 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 again measured. The infusion was then stopped and 15 minutes later, baseline values were again measured. 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.

Statistical analysis was done using Statview 5.0 (SAS Institute Inc, Cary, NC, U.S.A.) and Instat 2 (GraphPad Software Inc. San Diego CA, U.S.A.). For comparisons of the two treatments, a paired t test was used. The three controls were compared with ANOVA. For all probabilities, a two-tailed test was used with significance set at $P = 0.05$.

## RESULTS

The experimental protocol was completed in seven pigs. All pigs had a direct bronchial airway from the trachea to the right upper lobe and the final intubation with the double-lumen tube completely excluded the right lung. The results are presented as mean values with standard deviations.

### *Cardiac Output*

The control cardiac outputs ranged from 2.2 to 4.5 l/min. The percentage increase in cardiac output with dopamine ranged from 59%% to 123%, and with dobutamine from 42% to 204%.

### *Mixed Venous Oxygen Content*

Mixed venous oxygen content rose with all dopamine and dobutamine infusions. With dopamine it rose from a mean of 7.5 ml per 100 ml (SD 2.8 ml) to a mean of 9.3 ml per 100 ml (SD 2.8 ml). The mean increase was 29% (range 2 to 87%, $P$=0.043). The mean increase with dobutamine was from 7.0 ml per 100 ml (SD 2.1 ml) to a mean of 9.6 ml per 100 ml (SD 1.6 ml) with a mean increase of 44% (range 17% to 103%, $P$=0.0076).

Overall, the rise in venous oxygen content appeared to be linearly related to the increase in cardiac output (r=0.54, Figure 1).

### *Arterial Oxygen Saturation*

The control arterial oxygen saturation varied from 79.3% to 100%: the mean control saturation was 94.2±5.2%. The mean control saturations for the dopamine and dobutamine were 95.6±2.4% and 92.8±7.0% respectively ($P$=0.33). During dopamine infusion, the arterial saturations varied from 79.1% to 99.8%, and the mean saturation was 91.0±7.6%. The mean change in saturation was –4.7±6.3% ($P$=0.098). During dobutamine infusion, the mean arterial saturations varied from 79.1% to 100%, and the mean saturation was 89.9±7.2%. The mean change in saturation was -2.9±5.5% ($P$=0.21).

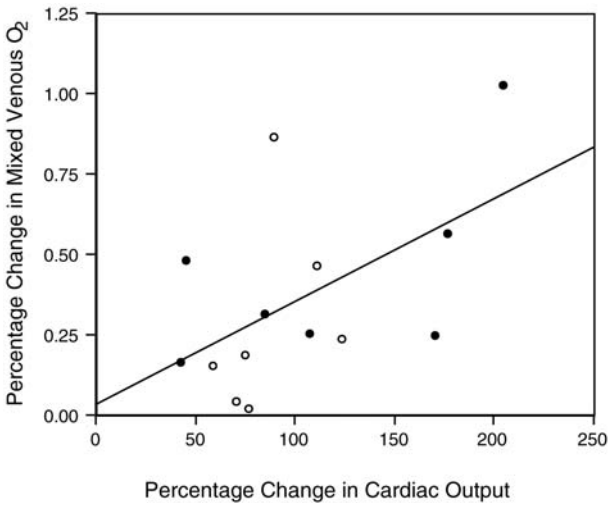


FIGURE 1: Relative change in mixed venous oxygen content with changes in cardiac output. There is a rise in mixed venous oxygen content as the cardiac output is increased. Regression line $\Delta Vo_2$= 0.003 ($\Delta$CO)+0.036. The dark dots are dobutamine stimulation and the open circles are dopamine.

### *Shunt*

For the whole group, the mean control shunt was 27.8±8.6%. After the administration of dopamine, the mean shunt increased to 42.1±9.5%. The mean difference between the mean control shunt and the mean shunt during dopamine infusion was 14.5±6.7% (paired t=5.7, $P$=0.0013, Figure 2).

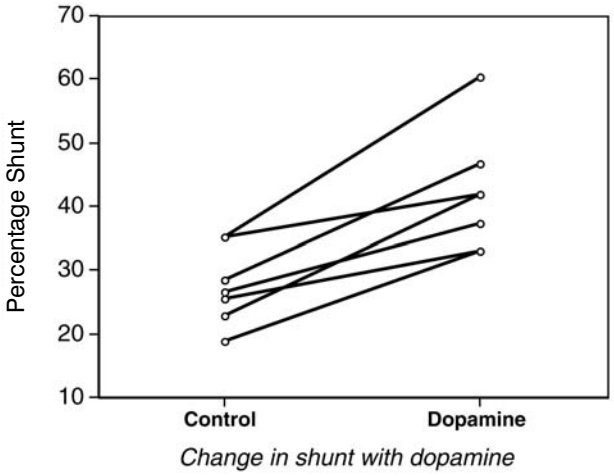


FIGURE 2: The effect of dopamine infusion on shunt. In all pigs the shunt increased. The mean increase was 14.5±6.7% (mean±SD).

The mean control shunt prior to the administration of dobutamine was 28.0±11.1%, which was not significantly different from the dopamine control ($P$=0.92). During the dobutamine infusion, the mean shunt increased to 45.4±15.0%, which was again not significantly different from the shunt during the dopamine infusion ($P$=0.62), but was significantly greater than the control shunt. The mean difference in shunt from control for the dobutamine infusions was 17.4±10.4% (paired t=4.4, $P$=0.0044, Figure 3).

### *Oxygen Consumption*

For the whole group, the mean control oxygen consumption was 180.8±43.8 ml/min. After the administration of dopamine, the mean consumption increased to 230.9±52.7 ml/min ($P$=0.016). The mean difference between control and the oxygen consump-

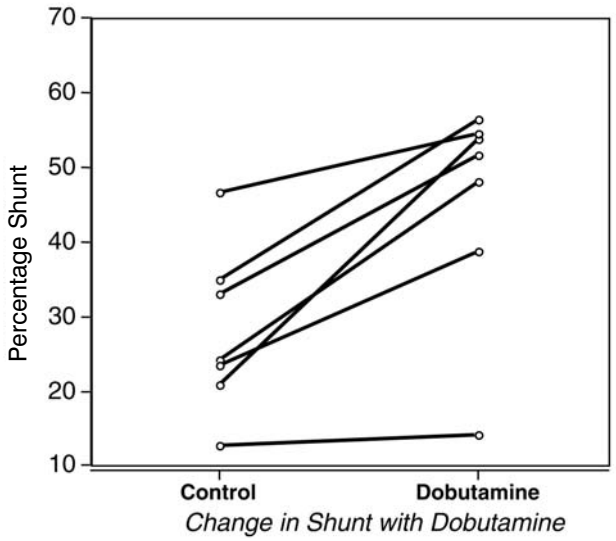


FIGURE 3: The effect of dobutamine infusion on the shunt. In all pigs the shunt increased. The mean increase in shunt was 17.4±10.4% (mean±SD).

tion during dobutamine infusion was similar at 61.7±48.6 ml/min (paired t=3.36, $P$=0.015). The combined results are shown in Figure 4.

*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 and oxygen consumption were not significantly different each of the three times. (For shunt, one-way ANOVA with repeat measures F=0.11, $P$=0.90; and for oxygen consumption one-way ANOVA with repeat measures F=0.30, $P$=0.75 respectively.)

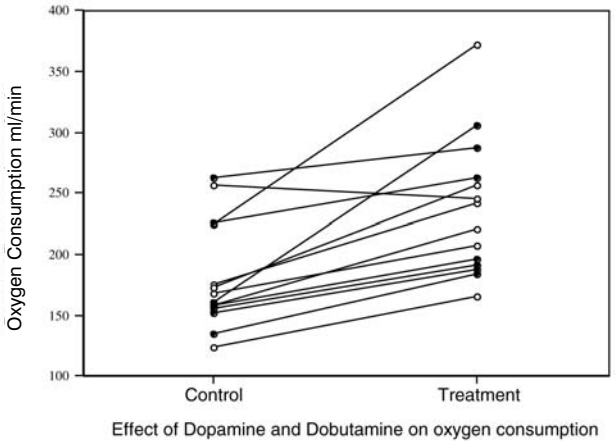


FIGURE 4: Change in oxygen consumption with dopamine and dobutamine infusions. The solid lines and solid dots show the control and dopamine treatment oxygen consumptions; the mean increase in oxygen consumption was 52.1±41.4 ml/min. The dashed lines and open circles show the control and dobutamine treatment oxygen consumption; the mean increase was 61.6±48.6 ml/min.

## DISCUSSION

It is clear that in this pig model, in spite of an improved mixed venous oxygen content, the use of either dopamine or dobutamine to boost cardiac output is associated with a significant increase in shunting which impedes any improvement in arterial oxygen saturation. Thus four possible agents stimulating cardiac output and thus arterial saturation have been shown not to achieve this goal. The increased shunt may be the result of strong inhibition of hypoxic vasoconstriction or a direct intra-pulmonary vasodilatation. Studies by Furman et al[2] and Marin et al[3] have shown that isoprenaline and dobutamine have pulmonary vasodilator properties that may inhibit hypoxic pulmonary vasoconstriction.

Although it is possible that other cardiac stimulants may be able to increase the cardiac output without the adverse effects, the present evidence suggests that most potent inotropes do increase oxygen consumption[4]. Of the presently available inotropic agents, even dopamine, which has been claimed not to increase oxygen consumption[5], did not improve oxygenation. Although neither the further desaturation with dopamine nor dobutamine treatment reached statistical significance, this might be clinically significant. A post hoc power analysis indicated that with the difference observed, 21 pigs would have to be treated for the difference to reach statistical significance.

Whether or not there is another inotropic agent that would avoid increased intrapulmonary shunting is open to question. However, it seems likely that any agent with significant beta-adrenergic activity would cause a similar degree of pulmonary vasodilatation, thus negating the ability of any improved venous oxygen content to achieve a higher arterial oxygen saturation.

The correlation between the increase in cardiac output and the increased shunt suggests that increasing cardiac output by the use of β-adrenergic agents will inevitably be offset by increases in shunt. The results of this study strongly suggest that any attempt to improve arterial saturation during one-lung anaesthesia by stimulation of cardiac output with catecholamines is unlikely to be beneficial. However, it should be borne in mind that these experiments were conducted in animals with healthy lungs, and with a large number of pulmonary segments not ventilated. It is possible that these results may not apply to quite the same extent in patients in whom the excluded

lung is extensively diseased. Conceivably, in such cases, where the collapsed lung may be minimally responsive to the vasodilator effects of inotropic agents, enhancement of cardiac output with inotropic support may benefit arterial oxygenation, through the increased mixed venous oxygen content that we have shown with all inotropes tested. The value of catecholamines with a greater vasoconstrictor effect remains to be investigated.

In conclusion, although enhancing the cardiac output with a catecholamine infusion should theoretically improve the arterial saturation during one-lung anaesthesia, our experiments in pigs do not support this hypothesis. As with isoprenaline and adrenaline[1], stimulation of cardiac output either with dopamine or dobutamine is associated with an increased shunt and therefore no improvement in arterial oxygenation. These two effects offset each other and prevent any beneficial effect in arterial oxygenation.

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