Effect of manual hyperinflation on haemodynamics in an animal model

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ABSTRACT Background and Purpose. Manual hyperinflation is a physiotherapy technique that improves static compliance and mobilizes secretions, but has the potential to alter haemodynamic function. The aim of the present study was to investigate the effects of manual hyperinflation on haemodynamic function in a healthy animal model, without the usual confounding effects inherent in an heterogeneous intensive care population. Method. The study used a within-subjects design, in an animal research theatre. Nine healthy sheep (eight Border Leicester, one Merino, mean weight 39.5 kg, standard deviation (SD) 1.6 kg) completed the study. The sheep were induced (thiopentane 15–20 ml), intubated, ventilated and surgically instrumented for an arterial line and pulmonary artery catheter. Anaesthesia was maintained by 1.5% halothane/oxygen. Manual hyperinflation was delivered for two minutes with a Mapleson C circuit, using a peak inspiratory pressure of 35cmH2O and an inspiratory:expiratory ratio of 2:1. Results. Mean tidal volume during manual hyperinflation was 294% (SD 22%) of the ventilator tidal volume. A paired Student’s t-test demonstrated that cardiac output (thermodilution method) decreased significantly (p<0.05) and systemic vascular resistance increased significantly (p<0.01) after manual hyperinflation. A repeated-measures analysis of variance (ANOVA) and a least-significant difference pairwise comparison revealed that mean arterial pressure and pulse pressure decreased significantly (p<0.01) and increased significantly (mean arterial pressure, p<0.05 and mean pulse pressure p<0.001) after the technique. Pulmonary artery pressure also increased significantly during manual hyperinflation (p<0.01). There were no significant effects on right atrial pressure, pulmonary artery occlusion pressure or heart rate. Conclusion. Significant haemodynamic changes occurred in this animal model. The increased intrathoracic pressure, applied for an increased period during inspiration, decreased cardiac output with compensatory vasoconstriction evident by the increased systemic vascular resistance and mean arterial pressure. The results suggest that there may be a decrease in cardiac output after increased positive pressure in subjects with normal cardiac and respiratory function.

Key words: animal model, cardiac output, haemodynamics, physiotherapy, sheep.
INTRODUCTION

Manual hyperinflation is a technique frequently used in the respiratory care of ventilated patients (Jones et al., 1992a; King and Morrell, 1992). It consists of disconnecting the patient from the ventilator and administering larger tidal breaths with a valve and reservoir bag. Manual hyperinflation has been shown to improve static and dynamic compliance (Jones et al., 1992b; Paratz et al., 2002), resolve atelectasis (Stiller et al., 1990) and result in increased suctioned secretions (Hodgson et al., 2000).

The term ‘hyperinflation’ implies any breath greater than tidal volume (Clement and Hubsch, 1968) and these authors recommend that the pattern of manual hyperinflation should comprise a long inspiration, an inspiratory plateau (to assist the recruitment of alveoli) and a fast expiration (to maximize mean expiratory flow rate).

In theory, adverse haemodynamic effects could result from this ventilation pattern (Conway, 1975); however, existing research on the haemodynamic effects of manual hyperinflation is difficult to evaluate. Previous studies (Henman and Guthrie, 1983; Preusser et al., 1988; Stone et al., 1991; Singer et al., 1994; Jellema et al., 2000) have not standardized the technique or personnel performing the technique, with the result that there is large variability in peak inspiratory pressure, tidal volume, positive end expiratory pressure, rate, inspiratory:expiratory ratio and FIO2 used in each study.

In addition, utilizing an intensive care population indicates that subjects will have differing pathology, lung compliance, volume status, myocardial dysfunction, sedation and inotropic agents. The determinants of cardiac output and contractility, as well as preload and afterload, are affected by volume status, acid base and electrolyte balance, the state of the myocardium and pharmacological agents. Several studies have also combined respiratory care techniques (Preusser et al., 1988; Stone et al., 1991; Jellema et al., 2000), including positioning and endotracheal suction, which make any changes difficult to attribute to manual hyperinflation alone.

Invasive haemodynamic monitoring, that is, pulmonary artery catheters, is commonly used in critically ill patients with septic or cardiogenic shock (Gimosair and Sprung, 1996). A patient with normal cardiac function would rarely, if ever, have a pulmonary artery catheter inserted; therefore, any opportunity to measure haemodynamic function during manual hyperinflation is limited. The use of an animal model permits the measurement of invasive haemodynamic data in a population with a normal cardiac function, and also lessens the variability found in a typical intensive care population.

The aim of the present study was to investigate the haemodynamic effect of manual hyperinflation in a healthy animal model, with the null hypothesis being that the technique would not significantly alter cardiac output, mean arterial pressure, systemic vascular resistance, pulmonary artery occlusion pressure, pulmonary artery pressure or pulse pressure.

METHOD

The study used a within-subjects design, in an animal research theatre. Ethical approval was obtained from the University of Queensland Animal Experimentation Ethics Committee and complied with the ‘Australian Code of Practice for Care and Use of Animals for Scientific Purposes by the NH&MRC/CSIRO/AAC’. The principles of laboratory animal care (NIH publication No. 86-23, revised 1985) were followed.
Nine sheep (eight Border Leicester and one Merino) were used for the study. The animals were in good health and suitable for vascular catheterization, with a mean weight of 39.5 kg (±1.6 kg) and mean age of 2.8 years (±1.2 years). The sheep were induced by intravenous injection of thiopentone (15–20 ml) and anaesthesia was maintained with halothane/oxygen, 1.5%. They were intubated with a size 8–10 FG endotracheal tube and ventilated with a Campbell ventilator (Ulco, Marrickville, NSW, Australia) with a tidal volume of 10 ml/kg, a respiratory rate of 10–14 breaths/min, a positive end expiratory pressure of 5 cmH₂O and an F₂O₂ of 0.4. The animals were then surgically instrumented for an arterial line and pulmonary artery catheter. An indwelling arterial line was inserted into the left carotid artery and connected to a pressure transducer and the VR-16 component V2206 (Electronics for Medicine, Bell and Howell, New York, USA).

The pulmonary artery catheter (American Edwards Laboratories, Irvine, CA) was introduced via a right internal jugular vein, advanced through the right heart and placed so that the distal lumen was in the pulmonary artery. Pulmonary artery occlusion pressure was measured by inflating the balloon on the tip of the catheter and was measured on the chart tracing at end-expiration. Cardiac output was determined by use of the thermodilution method (average of three means). Figure 1 details the method and timing of all the haemodynamic measurements.

Arterial blood gases were taken via the arterial line and analysed by the ABL620 Radiometer (Copenhagen, Denmark). Subjects were kept in the low range of normovolaemia with a mean pulmonary artery occlusion pressure of 7.6 mmHg (±1.7 mmHg). The sheep were allowed 30 minutes for haemodynamic stabilization once the surgical instrumentation had been completed.

**FIGURE 1:** Schematic detail of method and timing of recording of haemodynamic data. * = measured continuously; # = measured before and after manual hyperinflation; SAP = systolic arterial pressure; DAP = diastolic arterial pressure; MAP = mean arterial pressure; RAP = right atrial pressure; PAP = pulmonary artery pressure; PAOP = pulmonary artery occlusion pressure; CO = cardiac output; HR = heart rate.
The definition of haemodynamic stability before completing the baseline measurements was based on values of heart rate, mean arterial pressure, pulmonary artery occlusion pressure and cardiac output being in the normal range for sheep (Piper et al., 1996) and variability of less than 3% in measurements of mean arterial pressure and heart rate.

A Mapleson C circuit with expiratory valve (CIG DF 655, Medishield) and 2l reservoir bag (Rusch, Kernen-Rommelshausen, Germany) was used to hyperinflate the sheep manually. A pressure manometer (Mallinckrodt, VBM, Germany) and a Wright Respirometer (Clement Clarke International Ltd., London) were used in the circuit. Peak inspiratory pressure, tidal volume and minute volume were recorded during manual hyperinflation. Peak inspiratory pressure was limited to 35 cmH2O with the tidal volume during manual hyperinflation reaching 294% (±22%) of the set tidal volume. The sheep were disconnected from mechanical ventilation, manually hyperinflated for two minutes and reconnected to ventilation. The method of manual hyperinflation was a slow inspiration (2 s), inspiratory plateau (2 s), fast expiration (1 s) and pause for 1 s, giving a 2:1 ratio. Exhalation was complete and there was no positive end expiratory pressure generated within the circuit. The rate was 10 breaths per minute and the timing was to a strict count. One experienced operator (LA) performed the technique to minimize variability.

Two minutes’ recording of the measures were taken at baseline, during and after the intervention. All recording is detailed in Figure 1. The results were averaged for each time period. Pulse pressure, (pulse pressure = systolic artery pressure minus diastolic artery pressure) and systemic vascular resistance (systemic vascular resistance = mean arterial pressure minus right atrial pressure multiplied by 80 divided by cardiac output) were also calculated before and after manual hyperinflation.

Statistics

The results were calculated by use of SPSS (Version 6.0; SPSS, Chicago, IL). Data were tested for outliers, and the distribution and range of scores were examined to ensure that parametric statistics could be used. Mean changes scores, standard deviations (SD) and 95% confidence intervals (95% CI) were calculated before and after manual hyperinflation. A repeated-measures, one-way analysis of variance (ANOVA) was used with the independent variable time of measurement for pulmonary artery pressure, mean arterial pressure, pulse pressure and heart rate. When differences between variables were found a post hoc analysis using the least-significant difference model was used. Student’s t-test was used to establish whether there was a significant difference between measurements of cardiac output, pulmonary artery occlusion pressure and systemic vascular resistance before and after manual hyperinflation. A probability of $p<0.05$ was considered statistically significant. A standard deviation from a previous study (Patman et al., 1998) indicated that 13 subjects were needed to give a power of 80%. Owing to resource limitations, we were unable to continue beyond nine subjects; however, by use of the standard deviation from the cardiac output measures, power was calculated at 67% at this stage.

RESULTS

Table 1 shows the mean (SD) values for the variables of mean arterial pressure, pulmonary artery pressure, right atrial
pressure, heart rate and pulse pressure, whereas Table 2 contains the differences between each of the means for the three phases. Mean arterial pressure ($F(2,24) = 4.23, p=0.02$) and pulse pressure ($F(2,24) = 3.56, p=0.04$) decreased significantly during manual hyperinflation and increased afterwards. Pulmonary artery pressure increased during manual hyperinflation ($F(2,24) = 6.95, p=0.004$). No significant effects were found for right atrial pressure or heart rate.

Table 3 shows the mean (SD) differences for the measurements of cardiac output, pulmonary artery occlusion pressure and systemic vascular resistance before and after manual hyperinflation. Cardiac output decreased significantly after manual hyperinflation (Student’s $t$-test (8) = 2.66, $p=0.02$, whereas systemic vascular resistance increased significantly (Student’s $t$-test (8) = −5.36, $p=0.0006$). No significant effects were found for pulmonary artery occlusion pressure.

**DISCUSSION**

The manual hyperinflation procedure consists of using increased tidal volumes, a long inspiratory time, an inspiratory plateau and fast expiration to recruit atelectatic...
alveoli and to remove bronchial secretions. The technique has been found to alter haemodynamics (Henman and Guthrie, 1983; Preusser et al., 1988; Stone et al., 1991; Singer et al., 1994).

The main aim of the study reported here was to investigate the haemodynamic effects of manual hyperinflation in a model with very limited variability. By use of a healthy animal model it was possible to avoid the confounding effects of age, levels of sedation, state of the myocardium, inotropic agents, disease processes and lung compliance.

The most significant effects found were the decrease in mean arterial pressure and pulse pressure during manual hyperinflation; in cardiac output after the technique; and the rebound in mean arterial pressure and pulse pressure after manual hyperinflation. Pulse pressure is considered to be an approximate guide to cardiac output as it gives an indication of the size of the stroke volume (Abel and McCutcheon, 1979). The effects of increased intrathoracic pressure in an intubated patient have been described previously in a large study (Blackburn et al., 1973). Initially there is a compression of vessels in the pulmonary system, providing increased blood flow to the left ventricle, increasing its preload and therefore the stroke volume. After this period there is a reduction in stroke volume and blood pressure. This effect is offset by an increase in systemic resistance, that is, systemic vascular resistance. After the positive pressure is released, the stroke volume is restored, and there is an increase in restoration of cardiac output against a constricted circulation. This response is mediated by the baroreceptors and requires the compensatory neural pathways to be intact.

This hypothesis appears to mirror the results of the present study. Although cardiac output was not measured during the procedure, it is assumed it decreased as pulse pressure reflects what is occurring to stroke volume (Abel and McCutcheon, 1979). Mean arterial pressure initially decreased in response to this decrease and then rebounded after manual hyperinflation. Systemic vascular resistance also increased significantly after the technique, indicating

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pre-MHI</th>
<th>Post-MHI</th>
<th>Mean difference</th>
<th>Confidence intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO (1/min)</td>
<td>3.42 (0.94)</td>
<td>2.92 (0.60)*</td>
<td>0.49 (0.55)</td>
<td>0.06, 0.92</td>
</tr>
<tr>
<td>PAOP (mmHg)</td>
<td>7.6 (1.7)</td>
<td>7.8 (1.6)</td>
<td>–0.22 (1.3)</td>
<td>–1.29, 0.48</td>
</tr>
<tr>
<td>SVR (dynes/s/cm²)</td>
<td>1623.7 (299.6)</td>
<td>1954.3 (186.5)**</td>
<td>330 (185)</td>
<td>100.4, 559.6</td>
</tr>
</tbody>
</table>

MHI = manual hyperinflation; CO = cardiac output; PAOP = pulmonary artery occlusion pressure; MAP = mean arterial pressure; SVR = systemic venous resistance.

*p<0.05.

**p<0.01.
a vasoconstrictive response.

The baseline systemic vascular resistance was high in the animals in our study. The sheep may have vasoconstricted in response to the induction and anaesthesia, as these agents can cause an initial drop in blood pressure (Conway, 1975). However, the sheep still had compensation available, as there was an increase in systemic vascular resistance and mean arterial pressure after the application of increased positive pressure, that is, manual hyperinflation.

Increased pulmonary artery pressure is due to changes in pulmonary vascular resistance. This increase in right ventricular afterload may result in a decrease in left ventricular preload during manual hyperinflation. Large increases in tidal volume occurred, which may have caused alveolar distension and therefore changes in pulmonary vascular resistance. This in turn can decrease left atrial preload. Pulmonary artery occlusion pressure was only measured before and after the technique. Measurement during the technique may have shown a decrease in preload.

Previous studies have investigated haemodynamics during manual hyperinflation in subjects with septic shock who were receiving inotropic support (Jellema et al., 2000; Paratz et al., 2002) and post-operative cardiac surgery patients (Patman et al., 1998). Minimal changes in haemodynamics and a trend towards an increase in cardiac index were found. Myocardial depression is a feature of sepsis and if myocardial function in these subjects was less than adequate, positive pressure from manual hyperinflation can decrease preload and unload the left ventricle. Inotropic support may have also given some protection via a catecholaminergic effect. From our study, it would appear that subjects with normal cardiac function and compliant lungs may be more at risk of decreased cardiac output during manual hyperinflation than subjects with myocardial depression. With normal cardiac function, left ventricular stroke volume decreases in response to increased intrathoracic pressure (Pinsky et al., 1986). In addition, non-compliant lungs protect the circulatory system from changes in intrathoracic pressure, whereas healthy lungs permit the increased intrathoracic pressure to affect venous return.

The study reported here was planned to measure only one technique and therefore to give definite answers about the effect of manual hyperinflation on haemodynamics. Previous studies have included a variety of techniques, side-to-side positioning and endotracheal suction have often been investigated (Preusser et al., 1988; Stone et al., 1991; Jellema et al., 2000). Endotracheal suction, in particular, has been shown to result in profound haemodynamic alterations (Walsh et al., 1989) so conclusions about the haemodynamic effect of manual hyperinflation in these previous studies are questionable.

Earlier studies have found significant decreases in cardiac output (Singer et al., 1994) and mean arterial pressure (Henman and Guthrie, 1983). Singer and colleagues (1994), recording cardiac output with an oesophageal Doppler in an heterogenous intensive care unit population, found decreases in cardiac output 10 minutes after procedure, which was strongly correlated with increases in tidal volume. The subjects included in the study by Singer et al. (1994) would be considered unsuitable for disconnection from the ventilator and a manual hyperinflation procedure (King and Morrell, 1992), as a number were receiving high levels of inotropic support with an FIO2 >80%. Henman and Guthrie (1983) found a decrease in mean arterial pressure in hypovolaemic and vasodilated subjects.
Hypovolaemia and vasodilatation are factors associated with a drop in cardiac output on initiation of positive pressure.

In the present study, cardiac output may have decreased because the sheep were receiving an inhaled anaesthetic that has been shown to result in an adverse response to increased intrathoracic pressure (Hillman, 1986). This factor differs from a clinical intensive care population, but an anaesthetic was mandatory for ethics approval with animal work. A further limitation of the study is that arterial blood gases were not taken after the procedure. Arterial blood gases were taken purely to ensure that oxygenation, acid base balance and electrolytes were within normal limits. As there was a high tidal volume, hypocarbia may be the reason for the decrease in cardiac output.

Peak inflation pressures in the present study were kept at 35 cmH\textsubscript{2}O, which is accepted at present as a safe procedure in clinical practice (King and Morrell, 1992). As the sheep had excellent compliance, tidal volume during manual hyperinflation was 294\% (±22\%) of tidal volume given by mechanical ventilation, essentially 30 ml/kg. There is evidence that large tidal volumes may cause biotrauma and immune activation (Parker et al., 1993; Held et al., 2000) even in previously healthy lungs.

**IMPLICATIONS**

Manual hyperinflation is often used to prevent atelectasis in ventilated patients with no lung pathology; typical patient examples include head injuries, Guillain–Barré syndrome and post-operative patients. As lung compliance would be normal, these patients would be subjected to large tidal volumes, which may induce lung injury and sepsis. The results from the present study also suggest that positive pressure on a normal left ventricle is capable of decreasing output, so the majority of these patients would also be at risk of a decrease in cardiac output.

The anatomy of the sheep differs from humans in a few important aspects. The pulmonary arteries are smaller than in adult humans and therefore a pulmonary artery catheter will wedge in a more proximal vessel in the sheep. The wedged segment may be more likely to include lung regions where zone III conditions exists, thus causing a greater range in alveolar and pleural pressures from dependent to non-dependant lung regions. The effects of increased intrathoracic pressure on haemodynamics may therefore be exaggerated in the sheep.

The present study, however, still has relevance to clinical practice. The intensive care patient with normal lung compliance and normal cardiac function would rarely, if ever, have a pulmonary artery catheter inserted; therefore, any opportunity to measure haemodynamics during this commonly used technique would be limited. The study demonstrates what occurs during increased intrathoracic pressure in an essentially normal cardiopulmonary system. Examples of long-term patients who may have a normal cardiopulmonary system have been mentioned previously in this article.

Significant haemodynamic changes occurred in the animal model. Increased intrathoracic pressure, applied for an increased period during inspiration, decreased cardiac output with compensatory vasoconstriction evident by the increased systemic vascular resistance and mean arterial pressure. The increase in pulmonary artery pressure may have been due to the large tidal volume causing alveolar distension and increasing right atrial afterload.
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