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Acute effects of continuous rotational therapy on ventilation-perfusion inequality in lung injury

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Abstract *Objective:* To investigate ventilation-perfusion (V_A/Q) relationships, during continuous axial rotation and in the supine position, in patients with acute lung injury (ALI) using the multiple inert gas elimination technique.
Design: Prospective investigation.
Setting: Eighteen-bed intensive care unit in a university hospital.
Patients and interventions: Ten patients with ALI (PaO_2/FIO_2 ratio < 300 mm Hg) were mechanically ventilated in a pressure controlled mode and placed on a kinetic treatment table.
Measurements and results: Distributions of V_A/Q were determined 1) during rotation (after a period of 20 min) and 2) after a resting period of 20 min in the supine position. During axial rotation, intrapulmonary shunt (19.1 ± 15 % of cardiac output) was significantly reduced in comparison with when in the supine position (23 ± 14 %, $p < 0.05$), areas with "low" V_A/Q were not affected by the positioning maneuver. General V_A/Q mismatch (logarithmic distribution of pulmonary blood flow) was decreased during rotation (0.87 ± 0.37) in comparison with when the patient was in the supine position (0.93 ± 0.37, $p < 0.05$). Arterial oxygenation was significantly improved during continuous rotation (PaO_2/FIO_2 = 217 ± 137 mm Hg) as compared with in the supine position (PaO_2/FIO_2 = 174 ± 82 mm Hg, $p < 0.05$). The positive response of the continuous rotation on arterial oxygenation was only demonstrated in patients with a Murray Score of 2.5 or less, indicating a "mild to moderate" lung injury, while in patients presenting with progressive ARDS (Murray Score > 2.5), the acute positive response was limited.
Conclusions: Continuous axial rotation might be a method for an acute reduction of V_A/Q mismatch in patients with mild to moderate ALI, but this technique is not effective in late or progressive ARDS. Further studies including a large data collection are needed.

Key words Acute lung injury · Kinetic therapy · Ventilation-perfusion relationships · Intrapulmonary shunt · Multiple inert gas elimination technique

Introduction

Acute lung injury (ALI) is characterized by impaired arterial oxygenation due to ventilation-perfusion (V_A/Q) mismatch. The spectrum of therapeutic strategies includes special techniques of ventilatory management, pharmacologic interventions and changes in the patient's body position. In several studies [1–6], ventilation in the prone position was found to improve arterial oxygenation in comparison with the supine position in pati-

Table 1 Clinical characteristics of the patients

Patient	Age (years)	Diagnosis	Murray lung injury score	PaO_2/FIO_2 ratio (mm Hg) [before start of the study]	PEEP (cm H_2O)	FIO_2
1	30	Lung contusion	2.0	289	6	0.35
2	38	Urosepsis, pneumonia	2.0	195	6	0.4
3	68	Legionellosis following pulmonary embolism	3.0	96	9	0.65
4	36	Acute leukemia, pneumonia	4.0	89	12	0.8
5	66	Pneumonitis due to drug toxicity	2.7	85	6	0.7
6	73	Aortic aneurysm, pneumonia	2.0	160	7	0.55
7	71	Multitrauma, lung contusion	2.0	257	6	0.4
8	69	Peritonitis, pneumonia	2.7	143	6	0.5
9	47	Aspiration pneumonia due to intoxication	2.5	233	7	0.4
10	80	Pneumonia	3.0	122	8	0.6

ents presenting with the adult respiratory distress syndrome (ARDS), but all of these authors observed a group of patients who did not respond to the positioning maneuver with an improvement in pulmonary gas exchange. Using the multiple inert gas elimination technique (MIGET) for the assessment of V_A/Q-relationships, Pappert et al. [5] noted a decrease of intrapulmonary shunt in 8 of 12 ARDS patients after turning them from the supine to the prone position. The continuous axial rotation (kinetic therapy [KT]) is an alternative method for periodic positional changes [7]. KT facilitates the turning of patients using a motor-driven, oscillating bed. The kinetic treatment table rotates continuously on its long axis, through an arc of 124°, approximately every 7 min. In critically ill, immobilized patients, the combined incidence of atelectasis and pneumonia was significantly higher in conventionally treated patients in comparison with patients who were continuously turned on the kinetic treatment table [8]. Similar effects of a continuous postural oscillation on the risk of early pneumonia were found in intensive care patients presenting with non-traumatic critical illness [9] and in trauma victims [10]. Since the mechanism of a continuous axial rotation on pulmonary gas exchange is not known exactly, we investigated changes in V_A/Q-relationships during KT and in the supine position in intensive care patients who were mechanically ventilated due to ALI, using the multiple inert gas elimination technique. We hypothesized that KT would reduce V_A/Q inequality and would improve arterial oxygenation.

Patients and methods

Ten patients with ALI were prospectively and consecutively investigated. The study was performed at the University Hospital of Uppsala, Sweden, after approval by the local Ethics Committee and informed consent from the closest relatives. Clinical characteristics of the patients are given in Table 1. According to a recently published consensus [11], ALI was defined by a decrease in arterial oxygenation ($PaO_2/FIO_2 < 300$ mm Hg) and by the presence of bilateral infiltrates, demonstrated on chest roentgenogram. No patient had evidence of essentially unilateral pneumonia. In patient 3, pulmonary embolism had been treated successfully by lysis therapy. At the study time there was no sign of pulmonary perfusion stop in this patient.

The mean PaO_2/FIO_2 ratio before the start of the study was 156.7 ± 89 mm Hg and the calculation of a lung injury score [12] indicated the presence of a moderate to severe lung disease in all patients (mean lung injury score = 2.3 ± 0.96). Patients were mechanically ventilated in a pressure controlled mode (inspiratory/expiratory ratio 1 : 1, Servo 300, Siemens Elema, Lund, Sweden). Positive end-expiratory pressure (PEEP) ranged from 6 to 12 cm H_2O. Measurements were performed within 3 days after mechanical ventilation had begun. No patient had been placed in the rotational bed before the study. Routine clinical monitoring included a thermodilution pulmonary artery catheter and a femoral (or radial) artery catheter. After optimization of volume status (pulmonary capillary wedge presse 12–16 mm Hg) and ventilator settings, to achieve a stable hemodynamic situation and optimal gas exchange, the patients were placed on a kinetic treatment table (RotoRest, Kinetic Concepts, San Antonio, TX, USA).

All patients were deeply sedated during the study period. The sedation regimen and the ventilatory settings were not changed during the 24 h observational period. Two measurements were performed: 1) during rotation after a rotational period of 20 min by sampling exhaled gas and blood over a cycling period of the bed, 2) in the supine position (after a resting period in supine of 20 min). We decided to start measurements in the rotational mode, since measurements in the supine position performed im-

Table 2 Ventilator settings and ventilation data during axial rotation and in supine position. The arterial blood gas analyses are displayed

	Axial rotation	Supine	
Minute ventilation (l/min)	10.9 ± 3.2	10.9 ± 2.7	n.s.
Tidal volume (ml)	587 ± 103	566 ± 127	n.s.
PaO_2/FIO_2 (mm Hg)	217 ± 137	174 ± 82	$p < 0.05$
$PaCO_2$ (mm Hg)	39.5 ± 7	40.2 ± 8	n.s.

mediately after the placement procedure might have been falsified by the bed-placing maneuver itself. The maneuver of positioning the patient in the kinetic bed is usually accompanied by several lateral decubitus changes of the patient's body, which are necessary for an accurate and symmetrical placement.

Distributions of V_A/Q were determined, using the multiple inert gas elimination technique (MIGET [13, 14]). A mixture of six inert gases (sulfur hexafluoride, ethane, cyclopropane, enflurane, diethyl ether, acetone) was infused continuously at a constant rate of 3.5–4 ml/min into a peripheral vein. After 40 min, arterial, mixed venous blood and mixed expired gas samples (8 ml each) were taken simultaneously. Of each set of measurements, duplicate samples were treated separately. Inert gas concentrations were analyzed by gas chromatography (Hewlett Packard 5890, Series II, Rockville, Maryland, USA). Using a mathematical analysis, the inert gas data were transformed into a multicompartmental plot of blood flow and ventilation against V_A/Q. The result with the best fit of data "remaining sum of squares" (RSS [15]) of duplicate measurements was used for further statistical analysis.

From the V_A/Q distributions, data were presented for pulmonary perfusion as the mean and standard deviation of intrapulmonary shunt ($V_A/Q < 0.005$), "low V_A/Q" ($0.005 < V_A/Q < 0.1$), "normal V_A/Q" $0.1 < V_A/Q < 10$) and of the logarithmic distribution of pulmonary blood flow ($logSD_Q$). For alveolar ventilation, the data were expressed as the mean and standard deviation of "high V_A/Q" ($10 < V_A/Q < 100$), dead space ventilation ($V_A/Q > 100$) and of the logarithmic distribution of alveolar ventilation ($logSD_V$). Blood flow and ventilation were expressed in percent of cardiac output and minute ventilation, respectively.

Additionally, differences in the PaO_2/FIO_2 ratio between measurements during rotation and in the supine position (Δ-PaO_2/FIO_2) were compared with the severity of the lung disease (Murray lung injury score). The patients were then continuously rotated for at least 24 h after initiation of the study and the PaO_2/FIO_2 ratio was calculated again. Statistical analysis was performed using a SPSS software package. The data are presented as the mean ± standard deviation. Data were analyzed by the Wilcoxon matched-pairs signed-ranks test. The analysis between groups was performed by the Mann-Whitney U-test. The statistical significance was established at $p < 0.05$ in all cases.

Results

Ventilator settings and ventilation data are shown in Table 2. We found no differences in minute ventilation, tidal volume and $PaCO_2$ values during rotation compared with the supine position. Arterial oxygenation was significantly improved during continuous rotation compared with the following supine position. The results of the inert gas analysis and V_A/Q relationships during rotation and in the supine position are presented in Table 3. During KT, intrapulmonary shunt was significantly reduced in comparison with that in the supine position, and blood flow in the regions of "normal" V_A/Q increased during rotation. The mean RSS [15] was 1.21 ± 0.23, indicating a good reproducibility of the measurements. Areas with "low" V_A/Q were not affected by the continuous positioning maneuver. The overall V_A/Q mismatch, as expressed by the standard deviation of the logarithmic distribution of pulmonary blood flow ($logSD_Q$), was decreased during rotation in comparison with that in the supine position ($p < 0.05$).

Ventilatory indices ("high" V_A/Q, dead space, standard deviation of the logarithmic distribution of alveolar ventilation [$logSD_V$]) did not change during KT.

Table 3 Effects of a continuous axial rotation on pulmonary perfusion, alveolar ventilation and arterial oxygenation in comparison with supine position

	Rotation	Supine	Significance
Pulmonary perfusion (% of CI)			
Shunt (%) [$V_A/Q < 0.005$]	19.1 ± 15	23.0 ± 14	$p < 0.05$
"Low" V_A/Q (%) [$0.005 < V_A/Q < 0.1$]	2.3 ± 4	3.9 ± 6	n.s.
"Normal" V_A/Q [$0.1 < V_A/Q < 10$]	77.9 ± 17	72.6 ± 17	$p < 0.05$
$LogSD_Q$	0.87 ± 0.37	0.93 ± 0.37	$p < 0.05$
Alveolar ventilation (% of minute ventilation)			
"High" V_A/Q (%) [$10 < V_A/Q < 100$]	3.4 ± 5	4.7 ± 7	n.s.
Dead space ventilation [$V_A/Q > 100$]	32.8 ± 10	30.4 ± 9	n.s.
$LogSD_V$	0.84 ± 0.32	0.90 ± 0.36	n.s.

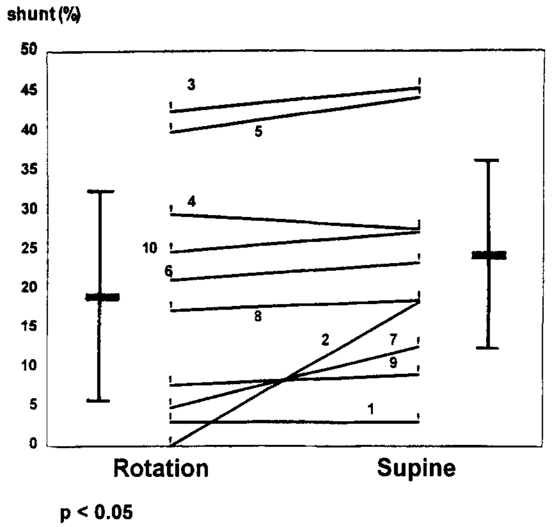

Fig. 1 Changes in intrapulmonary shunt (% of cardiac output) in ten patients during rotation and in supine position. The identification numbers of the patients are included

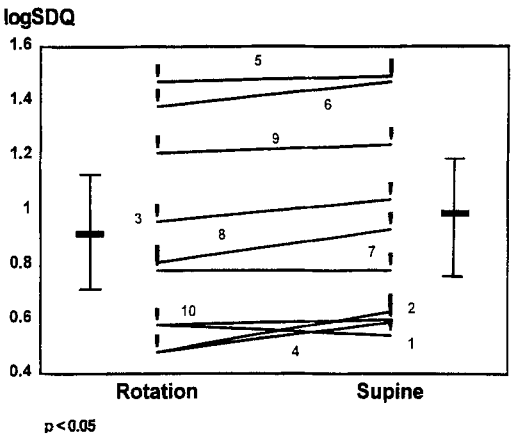

Fig. 2 Changes in the logarithmic distribution of pulmonary blood flow ($logSD_Q$) in ten patients during rotation and in supine position. The identification numbers of the patients are included

Arterial oxygenation after 24 h rotational treatment ($PaO_2/FIO_2 = 236 \pm 93$ mmHg) was significantly improved in comparison with the oxygenation before the start of the study ($p < 0.05$). Figure 1 presents the changes in shunt during rotation and in the supine position in the study patients. In Fig. 2 the changes in the distribution of pulmonary blood flow [$logSD_Q$] are shown. The hemodynamic effects of a KT treatment in comparison with the supine position are presented in Table 4. During rotation, no significant changes in heart rate, arterial pressure and cardiac index were observed.

The comparison between $\Delta PaO_2/FIO_2$ and the severity of lung injury (Murray score) is demonstrated in Table 5. We noted a statistically significant correlation

Table 4 Hemodynamic effects of a continuous axial rotation in comparison with supine position (*HR* heart rate, *MAP* mean arterial pressure, *CI* cardiac index)

	Rotation	Supine	Significance
HR (bpm)	90 ± 35	88 ± 34	n.s.
MAP (mm Hg)	68 ± 24	66 ± 23	n.s.
CI (l/m^2)	3.97 ± 1.7	3.82 ± 1.7	n.s.

Table 5 Differences in the PaO_2/FIO_2 ratio between measurements during rotation and in supine position (Δ-PaO_2/FIO_2) and the severity of lung injury (Murray Score)

	Murray Score	
	≤ 2.5 ($n = 5$)	> 2.5 ($n = 5$)
Δ-PaO_2/FIO_2 (mm Hg)	57 ± 32	8.6 ± 3 $p < 0.05$

between the variables ($p < 0.05$). In patients with a Murray score more than 2.5, which is by definition, associated with the presence of ARDS, we found no beneficial effect of the axial rotation compared with the effect in patients with lower Murray scores, indicating a "mild to moderate" lung injury.

Discussion

ALI is a common diagnosis for critically ill patients admitted to the intensive care unit. In a recent study [16], the overall hospital mortality rate of patients presenting with ALI was 58 %. The high mortality rate emphasizes the necessity for new treatment strategies. The importance of periodic changes in body position as a maneuver for improvement of gas exchange is well recognized and might be an established technique in most ICUs. The effect of the prone position in severe lung injury or ARDS was investigated in several studies [1–6]. In summary, an improvement of arterial oxygenation was observed in most patients while positioned prone, in comparison with when in the supine position. The mechanism seems to be a reduction of intrapulmonary shunt by a recruitment of previously atelectatic areas in the dorsal lung regions [17]. Nevertheless, the rate of non-responding patients, who did not react to positional changes or reacted with a deterioration of the arterial oxygenation, is reported to be 25–30 % [4, 5]. Furthermore, returning to the supine position reversed the beneficial effect in some patients.

Intermittent semi-decubitus posture is often used as a maneuver for the prevention of atelectasis and for improvement of oxygenation in intensive care patients. In a prospective investigation [18], Banasik et al. could not find a beneficial effect of intermittent lateral positioning on oxygenation in postoperative cardiac surgery patients. Similarly, Nelson and co-workers [19] did not observe an increase in PaO_2 by the simple lateral positioning of mechanically ventilated patients with symmetric lung disease.

The continuous rotation of patients was described as an alternative maneuver for systematic postural changes. Although the effect of a kinetic treatment on pneumonia and atelectasis formation in ICU patients has been studied [8–10], little is known of an acute effect of axial rotation treatment on V_A/Q relationships and on arterial oxygenation in patients with ALI. We therefore investigated the physiology of pulmonary gas exchange during KT using a technique which gives a detailed picture of V_A/Q ratio distributions. Our results demonstrated a mild reduction of intrapulmonary shunt during KT on an average 4 % of cardiac output and an increase of "normal" V_A/Q regions during a short observational period of 20 min. This effect was not accompanied by changes in tidal volumes and, hence, compliance. It could therefore be hypothesized that the change in intrapulmonary shunting may be a redistribution of pulmonary blood flow from non- to well-ventilated lung units during continuous rotation. Furthermore, the large range of FIO_2 in our patients (0.35–0.8) must be discussed as a possible effect on the degree of hypoxic pulmonary vasoconstriction.

However, a positive response to the maneuver in terms of pulmonary gas exchange was only demonstrated in those patients characterized by a Murray-Score of 2.5 or less. In ARDS patients, Pappert and co-workers observed a reduction of shunt in an average of 11 % of patients ventilated in the prone position [5]. In our patients we also noticed a reduced amount of dispersion in the logarithmic distribution of pulmonary blood flow (logSDa), which was not reported on in the paper by Pappert et al. The net effect of the reduced shunt and mismatch resulted in a similarly large improvement in oxygenation in our study ($\Delta PaO_2/FIO_2$: 43 mm Hg) as in the study by Pappert et al. ($\Delta PaO_2/FIO_2$: 48 mm Hg). The continuous moving of patients using a rotating bed seems to be more beneficial than intermittent semi-decubitus positioning, since it was demonstrated in recent studies [18, 19] that the maneuver of periodic positional changes by simply using pillows to prop patients off their backs failed to improve oxygenation in most patients.

In our study, we found no evident changes in cardiac index, mean arterial pressure or heart rate during rotation compared with when patients were in the supine position. Similarly, Nelson and co-workers [19] did not observe adverse effects on hemodynamics in hemodynamically stable patients during rotation. In contrast, a prolonged extreme lateral posture (62 °) might produce significant, and even adverse, effects on the cardiovascular system. In a recent study, Bein and co-workers [20] found an impairment of cardiovascular stability in critically ill, mechanically ventilated patients during extreme right decubitus position compared with the supine position, possibly due to altered distensibility of the right ventricle.

In our study, the less lung diseased patients showed better improvement of arterial oxygenation during rotational treatment than patients with high lung injury scores (> 2.5), which are commonly associated with the presence of ARDS. A progressive or late ARDS is characterized by structural changes of the parenchyma of the lung, such as a destruction of the alveolar architecture, emphysema-like lesions or progressive fibrosis [21, 22]. We conclude that the maneuver of continuous rotation is not effective in patients presenting with progressive ARDS. In contrast, ALI or early-stage ARDS is commonly characterized by a homogenous alteration of the vascular permeability and pulmonary edema. We suppose that the rotational maneuver is most useful in patients suffering from mild to moderate acute lung injury, which is characterized by a short anamnesis (< 4 days), by a moderate decrease in arterial oxygenation (PaO_2/FIO_2 ratio 200–300 mm Hg) and by signs of increased vascular permeability (chest X-ray, computed tomography). Nevertheless, the results of our study from a small data collection will have to be tested by multicentral studies to investigate clinical utility and the cost-effectiveness of oscillating beds in the treatment of acute lung injury.

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