Acute Respiratory Distress Syndrome

Pathophysiology, current management and implications for physiotherapy

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Key Words

Respiratory distress syndrome – acute, physical therapy, patient positioning, postural drainage, ventilation – mechanical

Summary

Acute respiratory distress syndrome (ARDS) is an intensive care condition first described more than three decades ago. Recent advances in the understanding of its pathology and management are reviewed. Of particular relevance to physiotherapists are the characteristic metabolic, haemodynamic and respiratory consequences of ARDS. These have implications for physiotherapy practice as chest physiotherapy has been demonstrated to have metabolic, haemodynamic and respiratory effects. Application of chest physiotherapy may exacerbate or attenuate these effects. However, there is a lack of research in this area.

On the other hand, body positioning has enjoyed much attention recently. The prone position is strongly advocated as an inexpensive alternative to new mechanical ventilatory modes in improving oxygenation.

Despite a large body of research on ARDS, it continues to carry a mortality rate of up to 70%. Therefore, there is a need for continuing research efforts on investigating its response to various therapeutic and supportive measures.

Introduction

Adult (or acute) respiratory distress syndrome (ARDS) was first described 30 years ago (Ashbaugh *et al*, 1967). In this original description, 12 out of 272 patients who were admitted to the intensive care unit (ICU) developed acute onset of severe dyspnoea, hypoxaemia, cyanosis and decreased respiratory system compliance, despite supplemental oxygen and mechanical ventilation. Since then, a large body of basic and clinical research on ARDS has been generated with the aim to elucidate its aetiology and to optimise its treatment. The purpose of this paper is to review the current understanding of ARDS, its pathophysiology, management and the implications for physiotherapy.

Definition

Ashbaugh and colleagues (1967) originally referred to the condition as 'acute respiratory distress'. In a subsequent report, this was described as 'adult respiratory distress syndrome' (Petty and Ashbaugh, 1971), a term that has since become established in the medical diagnostic vocabulary. Of the 12 patients described by Ashbaugh *et al* (1967), one was a child. It is now recognised that ARDS can affect not only adults, but also children (Katz, 1987; Davis *et al*, 1993; Sarnaik and Lieh-Lai, 1994; Paulson *et al*, 1995). It was therefore proposed that ARDS be considered as a form of acute lung injury (ALI) (Murray *et al*, 1988; Beale *et al*, 1993). The American-European Consensus Conference on ARDS recommended that ARDS, now known as acute respiratory distress syndrome, be defined as a 'syndrome of inflammation and increased permeability' associated with characteristic clinical, physiological and radiological changes (Bernard *et al*, 1994). These changes include an acute onset of deteriorating oxygenation expressed in terms of the ratio of arterial oxygen tension to fraction of inspired oxygen (PaO_2/FiO_2). For ARDS, the PaO_2/FiO_2 is defined as less than 200 mm Hg, while for ALI it is less than 300 mm Hg. Thus, ARDS is a more severe form of ALI. This definition also requires evidence of bilateral lung field infiltrates on chest roentgenograms; exclusion of left atrial or pulmonary capillary hypertension as a cause, though not necessarily the consequence, of ARDS; as well as the presence of one or more risk factors (Bernard *et al*, 1994).

Incidence, Mortality and Risk Factors

The reported incidence of ARDS varies between centres. The annual incidence per 100,000 population has been reported to be 1.5-3.5 cases in a Spanish island (Villar and Slutsky, 1989), 4.5 in the United Kingdom (Webster *et al*, 1988), 7.3-9.3 in Australia (Nolan *et al*, 1997) and 75.0 in the United States of America (Murray, 1977). While it is likely that the incidence may also depend on resuscitation practices among intensive care units (ICUs), a figure between 1.5 to 5.3 per 100,000 may be considered acceptable (Garber *et al*, 1996).

Despite much research on various treatment strategies, ARDS continues to carry a high mortality rate (Lee *et al*, 1994). Regardless of management practices, its mortality rate ranges from 30% to 70% (Ashbaugh *et al*, 1967; Villar and Slutsky, 1989; Lee *et al*, 1994; Doyle *et al*, 1995; DiRusso *et al*, 1995; Milberg *et al*, 1995; Nolan *et al*, 1997). Age was found to be associated with higher mortality in one retrospective study

(Suchyta *et al*, 1997) but this appeared to be due to higher incidence of withdrawal of support in older patients. The financial cost associated with ARDS is also high. In one report, it was estimated that the condition incurred a daily ICU charge of US$2,430 per patient per day (Bellamy and Oye, 1984). Seven out of 39 patients with ARDS survived in this survey. Survivors cost significantly less (US$1,683) than the non-survivors (US$2,760). The high costs and poor outcomes of ARDS are of great concern and a reason for ongoing therapeutic trials.

Sepsis, multiple blood transfusions, near drowning, pneumonia, aspiration of gastric contents, multiple trauma and drug overdose are some of the risk factors associated with ARDS (Pepe *et al*, 1982; Fowler *et al*, 1983; Hudson *et al*, 1995). Moreover, non-pulmonary organ system dysfunction appears to be prevalent in ARDS, with high incidence of renal, hepatic, gastrointestinal and cardiac involvement (Dorinsky and Gadek, 1989). Mortality is known to increase with the presence of risk factors, especially sepsis and non-pulmonary organ system dysfunction (Doyle *et al*, 1995). For example, sepsis accounts for about one-third (Montgomery *et al*, 1985) to over two-thirds (Hudson *et al*, 1995) of all ARDS deaths. Similarly, infection in the lungs, pleura or abdomen (Seidenfeld *et al*, 1986), gastric aspiration (Hudson *et al*, 1995) and non-pulmonary organ system dysfunction (Bell *et al*, 1983; Montgomery *et al*, 1985) have also been associated with high mortality in ARDS. Respiratory failure, however, accounts for only 10% of all ARDS deaths (Montgomery *et al*, 1985).

Pathogenesis and Pathophysiology

Direct and indirect lung injury may involve both the endothelium and epithelium (Bachofen and Weibel, 1977). Direct injury to the alveloar space and epithelium may be caused by infection, inhaled smokes or toxic gases and gastric aspiration. Indirect injury, primarily to the endothelium, is initiated by a series of events termed systemic inflammatory response (SIR). A variety of systemic conditions such as infection (sepsis), pancreatitis, multiple trauma and haemorrhagic shock may trigger SIR (ACCP, 1992). The outcome of lung injury is an inflammatory response characterised by increased cell membrane permeability, a subsequent capillary leak of high protein exudate into the interstitium and alveolar spaces (that is, acute non-cardiogenic pulmonary oedema), and a resultant increase in extravascular lung water (Fein *et al*, 1979).

There are three overlapping stages of ARDS, described as early (duration up to a week), intermediate (one to two weeks) and late (over two weeks) (Gattinoni *et al*, 1994). During the early stage of ARDS, there is marked increase in pulmonary vascular permeability (Calandrino *et al*, 1988). This increase has been shown to be homogeneous, resulting in non-gravitational distribution of acute pulmonary oedema in the interstitium and alveolar spaces (Pelosi *et al*, 1996). Histologically, there may be hyperaemia, engorged capillaries, interstitial and intra-alveolar haemorrhage and oedema with areas of alveolar atelectasis (Ashbaugh *et al*, 1967; Lamy *et al*, 1976).

There is a large number of inflammatory cells, such as neutrophils, mononuclear cells, pulmonary intravascular macrophages and platelets. A combination of various inflammatory cells, humoral mediators and nitric oxide (NO) metabolism may be involved in causing the inflammatory response and its sequelae (Fulkerson *et al*, 1996). Macrophages and platelets are involved in the release of mediators such as cytokines, products of arachidonic acid metabolism, oxygen free radicals and complements such as C5a (Rinaldo and Rogers, 1982). Cytokines such as tumour necrosis factor-alpha (TNF-α) and interleukins (ILs) are elevated in plasma and bronchoalveolar lavage fluid in patients with ARDS (Nash *et al*, 1991; Suter *et al*, 1992; Meduri *et al*, 1995). They cause neutrophil adhesion on the endothelium, thus potentiating the inflammatory responses (Wortel and Doerschuk, 1993). The toxic reactive oxygen species, produced or enhanced by high FiO_2 and reperfusion of hypoxic tissues, also mediate lung injury (Beale *et al*, 1993). Pulmonary vasoconstriction occurs as a result of alveolar hypoxia and circulating vasoactive substances (Zapol *et al*, 1977; Zapol and Snider, 1997; Greene, 1986; Artigas *et al*, 1987) such as arachidonic acid products, platelet-activating factors and complements. Inducible NO synthase is an enzyme found in both epithelium and endothelium which produces NO in response to cytokines and endotoxin (Barnes and Belvisi, 1993). Excess NO may cause further capillary leak and plasma exudation.

In the first few hours of an animal model of lung injury, 20–25% of the increased extravascular lung water has been shown to drain into the pleural space, causing pleural effusion (Wiener-Kronish *et al*, 1988). Radiologically, there is evidence of diffuse consolidation, pleural effusions (Aberle and Brown, 1990) and about 30% incidence of pneumothorax (Gattioni *et al*, 1994). During this stage, the patient becomes progressively dyspnoeic and tachypnoeic, often requiring ventilatory assistance.

During the intermediate stage, the lungs become heavier and may be two to three times the normal

lung weight (Gattioni *et al*, 1988a). The weight of the oedematous lungs exerts a vertical gradient of decreasing transpulmonary pressure, causing compression atelectasis of lung units in the dependent regions (Gattinoni *et al*, 1988a; Pelosi *et al*, 1996). As the oedema accumulates, fibrin is formed, causing thrombotic obstruction in the pulmonary vessels and resulting in pulmonary arterial hypertension (PAH) (Greene, 1986; Artigas *et al*, 1987). An increased right ventricular afterload is associated with PAH (Coetzee *et al*, 1996) and compensatory Frank-Starling mechanism operates to maintain right ventricular stroke volume (Dhainaut and Brunet, 1990). Poor right ventricular contractility, as in septic shock, may undermine this mechanism, resulting in right ventricular failure (Dhainaut and Brunet, 1990). Surfactant depletion and abnormalities have also been observed (Petty *et al*, 1979; Seeger *et al*, 1990; Li *et al*, 1991) and noted to correlate with the severity of ARDS (Pison *et al*, 1989). This surfactant dysfunction may contribute to the decrease in lung compliance, which has been found to be significantly lower than that in the early stage (Gattinoni *et al*, 1994).

The late ARDS stage is marked by widespread lung damage. Histologically, there is diffuse fibrosis (Lamy *et al*, 1976) and presence of hyaline membranes (Ashbaugh *et al*, 1967). Significant decrease in respiratory compliance and an increase in intrapulmonary shunts, dead space ventilation (Gattinoni *et al*, 1994) and airway resistance have been reported (Pelosi *et al*, 1995) although the latter is reversible by nebulised salbutamol (Morina *et al*, 1997). The increasing fibrotic changes may be responsible for the alterations in gas exchange and lung mechanics. The incidence of pneumothorax was reported to be 87% (Gattinoni *et al*, 1994). Often sepsis or infection is superimposed in the late stage of ARDS, and may be associated with high mortality rate.

Gattinoni and colleagues (1993) have used computed tomographic scans to characterise the lung structure in ARDS. Previously, ARDS was believed to be diffuse lung damage with a homogeneous and generalised distribution of atelectasis and damage to the alveolar-capillary barrier (Maunder *et al*, 1986). Gattinoni and colleagues (1988a, 1991) have however demonstrated that most of the lung collapses were found in the dependent zones. Based on these and other studies (Maunder *et al*, 1986; Gattinoni *et al*, 1987, 1988b, 1993), three areas in ARDS lungs have been distinguished: (1) an area of irreversibly damaged lung units; (2) an area of relatively recruitable collapsed alveoli; and (3) a very small area of normal undamaged alveoli. These undamaged lung units have been termed the 'baby lung' because they occupy a very small proportion, approximately 15 to 20%, of normal adult lung (Gattinoni *et al*, 1988a).

The oxygen transport system is also altered in ARDS. Normally when oxygen delivery (DO_2) to the tissues decreases, as it does in ARDS (Meade *et al*, 1994), oxygen consumption (VO_2) remains constant while tissue oxygen extraction increases. When DO_2 decreases to a critical level, VO_2 will then decrease linearly as DO_2 decreases. This is known as physiological dependence of VO_2 on DO_2. In ARDS, a 'pathological' dependence of VO_2 on DO_2, a linear relationship between these two variables, has been noted whereby oxygen extraction does not increase with decreasing DO_2 (Knox, 1993; Russell and Phang, 1994). Furthermore, DO_2 is caused by decreased cardiac contractility rather than preload and afterload (Stelzer *et al*, 1994a). Therefore, strategies to enhance DO_2 by inotropes and catecholamines have been used (Yu *et al*, 1995). However, calculation errors in the determination of VO_2 and DO_2 have been shown recently to account for the linear relationship established by previous studies (Hanique *et al*, 1994; Phang *et al*, 1994; Stelzer *et al*, 1994b). Nevertheless, at least one recent study, using direct measurements by indirect calorimetry, has demonstrated a VO_2-DO_2 linear relationship in patients with ARDS and sepsis (Yu *et al*, 1996).

Management: Current Practices

Lack of controlled randomised trials of specific therapeutic strategies explains why the current principle of management is still largely supportive (Kolleff and Schuster, 1995). The main goals of supportive treatment are to ensure adequate gas exchange and tissue perfusion, while minimising any possible iatrogenic or secondary lung injury. Treatment of specific predisposing and risk factors is also a goal in the overall management of ARDS.

Mechanical Ventilation

The initial settings, the application of positive end-expiratory pressure (PEEP) and various types of ventilatory modes have been the topics of many theoretical speculations and fewer investigations of rigorous designs. The application of increasingly high levels of PEEP recruits previously collapsed alveoli; while low levels of PEEP distend and aerate normal undamaged alveoli (Gattinoni *et al*, 1987, 1988b, 1993). But at high levels of PEEP, the normal alveoli have been found to be overly distended (Gattinoni *et al*, 1993). Overdistention, or 'volutrauma' has been shown to be associated with pneumothorax in ARDS (Finfer and Rocker, 1996). High supplemental oxygen therapy has also been used, but the ensuing

oxygen toxicity is well known (Jenkinson, 1993). The iatrogenic effects of high levels of PEEP and FiO_2 have resulted in the development of many different ventilatory strategies.

One strategy to avoid volutrauma to the 'baby lung' employs the use of lower tidal volumes (as low as 6 ml/kg body weight) and/or ventilatory rate, thus permitting the arterial carbon dioxide tension to rise. Permissive hypercapnia aims to reduce peak airway distending pressure (and hence volutrauma) associated with high tidal volume (Kacmarek and Hickling, 1993; Tuxen, 1994). This has been shown to decrease the incidence of pulmonary infection (Lee *et al*, 1990), improve respiratory system compliance (Leatherman *et al*, 1991), decrease minute ventilation (McIntyre *et al*, 1994), increase oxygen delivery (Kiiski *et al*, 1992; Thorens *et al*, 1996), facilitate earlier ventilator weaning (Amato *et al*, 1995), prevent a decrease in cardiac output (CO) (Leatherman *et al*, 1991; Kiiski *et al*, 1992), and cause lower mortality (Hickling *et al*, 1990). However, it has also been associated with elevated cardiac index, intrapulmonary shunt and mean pulmonary arterial pressure (Thorens *et al*, 1996).

Another strategy commonly used to reduce the peak airway pressures is inverse-ratio ventilation (IRV) where the inspiration:expiration (I:E) ratio is increased. However, recent controlled randomised trials have shown no additional benefits, in terms of oxygenation, lung mechanics and haemodynamics, over the conventional volume-cycled ventilation with normal I:E ratio (Mancebo *et al*, 1994; Mercat *et al*, 1997). In fact, IRV has been found to decrease CO (Mercat *et al*, 1997).

Airway pressure release ventilation is another form of ventilatory mode that aims to reduce the peak airway pressure. It is a form of continuous positive airway pressure (CPAP) for spontaneously breathing patients, with periods when the airways rapidly depressurise allowing expiratory gases to empty and fresh gas to refill the airways to the pre-set CPAP. It has been shown to have lower peak airway pressure, higher oxygenation and lower intrapulmonary shunt when compared to volume-cycled IRV (Sydow *et al*, 1994).

Extracorporeal ventilatory support has been tried in some centres. Prospective clinical randomised trials have shown that both extracorporeal membrane oxygenation (Zapol *et al*, 1979) and extracorporeal carbon dioxide removal (Morris *et al*, 1994) offered no additional benefits over conventional ventilatory support.

Partial liquid ventilation with perfluorocarbons has been used and studied in some centres. The lungs are filled with perfluorocarbon to functional residual capacity (FRC) while gas ventilation is effected by conventional mechanical ventilator. Surface tension is reduced with this approach, thereby recruiting more lung volume and facilitating better gas exchange (Hernan *et al*, 1996). Studies involving both animal models (Hernan *et al*, 1996; Hirschl *et al*, 1996a) and patients with severe ARDS on extracorporeal support (Hirschl *et al*, 1996b; Kazerooni *et al*, 1996) have shown improved gas exchange and lung mechanics without any complications.

Fluid Management

Fluid therapy has been a topic of much debate within the medical community (Schuster, 1995; Sporn, 1996). Some studies have shown lower mortality and improved outcomes of fluid support to increase DO_2 to supranormal states (Shoemaker *et al*, 1988; Yu *et al*, 1993), while others have shown better outcomes with fluid restriction (Mitchell *et al*, 1992). It has been suggested that fluid therapy is best if individually tailored (Fulkerson *et al*, 1996).

Pharmacological Interventions

Pharmacological interventions aim to interfere with the inflammatory process, reduce PAH and replenish surfactant. Recent randomised controlled trials have shown better oxygenation, reduced levels of inflammatory markers or improved survival with pharmacological interventions, including surfactant replacement (Weg *et al*, 1994; Gregory *et al*, 1997); antioxidants such as N-acetylcystein and procystein (Bernard *et al*, 1997); vasolidator such as nitric oxide (Walmrath *et al*, 1996; Doering *et al*, 1997) and prostacyclin (Walmrath *et al*, 1996); substances which enhance the hypoxic pulmonary vasoconstriction such as phenylephrine (Doering *et al*, 1997) and almitrine (Wysocki *et al*, 1994; Benzing *et al*, 1997; Jolliet *et al*, 1997); as well as inflammatory mediator-inhibitors such as prostglandins E_1 (Abraham *et al*, 1996). Corticosteroids have been shown to have no effect on improving survival in one randomised clinical trial (Bernard *et al*, 1987). Similarly, gut decontamination has not been found effective in reducing the incidence of ARDS (Cerra *et al*, 1992). Immunological therapy by administration of anti-endotoxin antibody (Bigatello *et al*, 1994) as well as cytokine antagonists (Opal *et al*, 1997) do not appear to improve survival when compared with conventional approaches.

Body Positioning

It has been suggested that the upright position could be important in improving the FRC in ARDS, a condition with a reduced FRC (Dean, 1996a).

The aim of body positioning in ARDS is to use gravity to optimise the ventilation-perfusion ratio, thereby improving gas exchange and oxygenation. However, to date, there has been no research evidence in favour of the upright position for people with ARDS. One study reported that PaO_2/FiO_2 remained unchanged when the semi-recumbent position was compared to the supine position in ARDS patients (Bittner *et al*, 1996). Moreover, respiratory compliance was reduced in the semi-recumbent compared to the supine position in this study.

The lateral decubitus position has been shown consistently to improve oxygenation (PaO_2 and/or PaO_2/FiO_2) in intubated and ventilated ICU patients with acute respiratory failure due to unilateral lung involvement (Ibãnez *et al*, 1981; Prokocimer *et al*, 1983; Rivara *et al*, 1984; Gillespie and Rehder, 1987). There is no clear advantage of this position for patients with radiographic appearance of bilateral lung field infiltrates (Nelson and Anderson, 1989). Furthermore, in patients with ARDS superimposed with marked SIR and moderate right ventricular dysfunction, the lateral decubitus position for just 15 minutes has been shown to cause significant haemodynamic changes (Bein *et al*, 1996). Left side lying appears to induce increased pre-load resulting in higher than normal CO; while right side lying causes a significant decrease in pre-load and right ventricular end-diastolic volume with a resultant systemic hypotension (mean arterial pressure fell from 85 mm Hg in supine to 72 mm Hg) (Bein *et al*, 1996). Thus, in applying the lateral decubitus position in patients with ARDS, it is important to be aware of and to monitor the haemodynamic variables, especially where CO may be compromised.

The prone position has been found to cause better arterial oxygenation in patients with ARDS (Piehl and Brown, 1976; Douglas *et al*, 1977). Since 1988, there has been a growing interest in the prone position (Langer *et al*, 1988; Gattinoni *et al*, 1991; Brüssel *et al*, 1993; Pappert *et al*, 1994; Hörmann *et al*, 1994; Murdoch and Storman, 1994; Vollman and Bander, 1996; Chatte *et al*, 1997; Stocker *et al*, 1997; Fridrich *et al*, 1997; Mure *et al*, 1997). All except four of these studies involved manual turning of the patients into prone, usually involving three to four medical, nursing or auxillary staff (see table). All except one study (Vollman and Bander, 1996) did not randomise the assignment of patients into the supine (control) and prone position. Despite the lack of randomised trials, the prone position has consistently resulted in higher oxygenation in all studies (see table), reduced intrapulmonary shunts (Brüssel *et al*, 1993; Pappert *et al*, 1994; Hörmann *et al*, 1994; Fridrich *et al*, 1997), lowered mortality (Stocker *et al*, 1997) and decreased FiO_2 (Brüssel *et al*, 1993; Mure *et al*, 1997). No haemodynamic complications have been reported (Gattinoni *et al*, 1991; (Brüssel *et al*, 1993; Pappert *et al*, 1994; Hörmann *et al*, 1994; Murdoch and Storman, 1994; Vollman and Bander, 1996; Chatte *et al*, 1997). However, dependent oedema in the face is to be expected (Douglas *et al*, 1977; Brüssel *et al*, 1994; Chatte *et al*, 1997; Fridrich *et al*, 1997; Mure *et al*, 1997). A semi-prone position has also been described in five case studies (Schmitz, 1991) with similar results.

Animal models of ALI have provided some explanations for these observations. A re-distribution of regional ventilation is likely to occur in adopting the prone position. Transpulmonary pressure exceeding airway opening pressure was observed to increase in the non-dependent lungs in canine models of lung injury (Lamm *et al*, 1994). Increased normal ventilation-perfusion units in the dorsal lung regions (Lamm *et al*, 1994) and reduced shunt perfusion (Albert *et al*, 1987) were shown to account for the improvement in oxygenation in patients lying prone. Furthermore, in the prone position, the weight of the heart, the mediastinum (Margulies and Rodarte, 1990) and the upper abdomen (Liu *et al*, 1990) no longer compress the underlying compromised lungs as in the supine position.

Therefore, it appears that there is quite strong evidence of enhanced oxygnation in ARDS patients placed in the prone position. Further investigations should focus on the effect of upright position, the optimal frequency and duration of the prone position, and the cost-effectiveness of this position when compared to the other modalities to improve oxygenation.

Finally, the effect of continuous turning, or 'kinetic therapy' has been investigated in Europe and North America (Gentiello *et al*, 1988; Choi and Nelson, 1992; Pape *et al*, 1994). A meta-analysis of research studies on kinetic therapy in critically ill patients appeared to suggest that this treatment modality had no significant effect on reducing the incidence of ARDS in a pooled sample size of 419 patients across five studies (Choi and Nelson, 1992). Pape *et al* (1994) compared a prospective cohort of post-trauma ARDS patients subjected to continuous turning with a historical cohort of ARDS patients who had been nursed only in the supine position. Significant improvement in PaO_2/FiO_2 with an accompanying decrease in pulmonary shunt was reported. The extravascular lung water was also significantly lower in the 'kinetic' group than the 'supine' control group. There were no significant

Effects of the prone position in patients with ARDS

Studies	*No of subjects*	*Manual or mechanical turning*	*Duration of position (hours)*	*Outcomes*	
				Risks	*Benefits*
Piehl and Brown (1976)	5	Mechanical	Not stated	Not studied	PaO_2↑ Secretions ↑ in three cases
Douglas *et al* (1977)	6	Both	4 and 33	CO↑ in two patients Two had periorbital and conjunctival oedema	PaO_2↑ in prone but returned to baseline when supine. Secretions ↑
Langer *et al* (1988)	13	Manual	2	None observed	PaO_2↑ in eight patients
Gattinoni *et al* (1991)	10	Manual	⅙	No haemodynamic changes	PaO_2 and Q_s/Q_t – no change. CT scan showed ↑ densities (atelectasis) in dependent regions, regardless of positions
Brüssel *et al* (1993)	10	Manual	10-42	No haemodynamic changes. Four had lip/eyelid oedema. Five had pressure bruises on forehead and anterior chest wall	PaO_2, Sa_2/O_2 and Pa/FiO_2↑ $P_{(A-a)}O_2$, Q_s/Q_t and FiO_2↓
Pappert *et al* (1994)	12	Manual	2	No haemodynamic changes	PaO_2↑ in eight patients in prone but returned to baseline when supine. Q_s/Q_t, ↓
Hörmann *et al* (1994)	7	Mechanical	12 over 6½ days	No haemodynamic changes	Q_s/Q_t, ↓ initially during prone only, but also in supine 2nd day onwards. F_iO_2 ↓. CT scan – clearance of atelectasis
Murdoch and Storman (1994)	7	Manual	½	No haemodynamic changes	SaO_2↑ in prone but returned to baseline when supine
Vollman and Bander (1996)	15	Mechanical	⅓	No haemodynamic changes	Overall PaO_2↑; $P_{(A-a)}O_2$↓
Chatte *et al* (1997)	32	Manual	4	No haemodynamic changes: Two had SpO_2↓ >5%. Two had vascular lines removed/compressed. One had arrhythmia One accidentally extubated causing mild cutaneous and mucosal damage	78% had PaO_2/FiO_2 ↑: more than half of these maintained improvements on return to supine
Stocker *et al* (1997)	25	Manual	¾	Not studied	PaO_2/FiO_2 and $P_{(A-a)}O_2$↑. Mortality 12%< comparable groups reported elsewhere
Fridrich *et al* (1997)	20	Manual	⅓ each turn; total 96 after four turns	Loss of endotracheal tube and central venous access. Shoulder and hip contractures. Facial oedema	Improvement up to 4th prone turn. PaO_2/FiO_2 - ↑; $P_{(A-a)}O_2$ - ↓ and Q_s/Q_t - ↓
Mure *et al* (1997)	13	Manual	Individualised 2 to 36 at one time	One endotracheal tube dislocated. No other serious side effect	PaO_2/FiO_2 - ↑, $P_{(A-a)}O_2$↓ and FiO_2 ↓

FiO_2 = fraction of inspired oxygen; ↑ = increase; ↓ = decrease; CT scan = computed tomographic scan; CO = cardiac ouput; SaO_2 = oxygen satuation; PaO_2/FiO_2 = arterial oxygenation tension to fraction of inspired oxygen ratio; PaO_2 = arterial oxygen tension; $P_{(A-a)}O_2$ = alveloar-arterial oxygen difference; Q_s/Q_t = interpulmonary shunt.

differences in the haemodynamic variables between both groups. The authors speculated that the improvements could be due to better drainage and removal of bronchial secretions, re-inflation of collapsed dependent alveoli, mobilisation of interstitial fluid into the capillary system to arrest pulmonary oedema and optimisation of the ventilation-perfusion ratio in previously shunted areas (Pape *et al*, 1994). Kinetic therapy, therefore, appears to have short-term clinical benefits but it does not reduce the incidence of ARDS.

The Role of Physiotherapy

The role of physiotherapy in modifying or exacerbating the inflammatory responses in ARDS has never been investigated. Some, if not the majority, of the inflammatory processes in ARDS are also found during exercise. As a stressor to the immune system, strenuous aerobic and eccentric exercises in top athletes were found to increase significantly the production of cytokines, such as TNF-α and the ILs, both during and after exercises (Cannon *et al*, 1991; Northoff and Berg, 1991; Kvernmo *et al*, 1992; Rivier *et al*, 1994). This increase in plasma cytokines has been implicated as the source of symptoms, such as fever, following intense exercise bouts (Northoff and Berg, 1991). Physiotherapy has been described as a form of stressor in the ICU setting (Weissman and Kemper, 1993). Positioning and mobilisation have also been advocated as a form of physical stressor in the ICU setting to combat the adverse effects of bed rest (Dean, 1996b). However, the effects of physiotherapy as an ICU stressor on the immune system and the inflammatory response in ALI and ARDS can so far only be inferred from the research literature on exercise immunology.

Physiotherapy, in terms of chest wall percussion and vibration as well as manual hyperinflation, to enhance mucociliary clearance in patients with ARDS has also never been studied, although it has been suggested to be of value (Takala, 1997). Nevertheless, a fair number of researchers have documented adverse metabolic, haemodynamic and respiratory effects of these techniques. Since ARDS has potential or known metabolic, haemodynamic and respiratory deficits, application of physiotherapy techniques must be based on weighing the risks-and-benefits scale. Any combination of postural drainage with or without manual techniques of either percussion, vibration and/or suctioning has been shown to significantly increase VO_2 (Weissman *et al*, 1984; Swinamer *et al*, 1987; Klein *et al*, 1988; Weissman and Kemper, 1993; Harding *et al*, 1994; Dean *et al*, 1996), cause cardiac arrhythmias (Hammon *et al*, 1992), elevate circulating catecholamines (Aitkenhead *et al*, 1984), increase rate-pressure product and CO (Aitkenhead *et al*, 1984; Weissman *et al*, 1984; Klein *et al*, 1988; Weissman and Kemper, 1993; Harding *et al*, 1993, 1994, 1995; Cohen *et al*, 1996) and reduce PaO_2 (Huseby and Hudson, 1976; Tyler *et al*, 1980; Connors *et al*, 1980; Harding *et al*, 1994). Manual hyperinflation has also been shown to decrease CO (Singer *et al*, 1994), which may further compromise an already poor DO_2 state in ALI and ARDS. Furthermore, tissue extraction is said to be the main mechanism to compensate for the increase in VO_2 during and following chest physiotherapy, as in exercise (Weissman and Kemper, 1991, 1993). In ARDS, however, any increase in VO_2 will require an increase in DO_2 instead of tissue extraction (Knox, 1993). It should also be recognised that any of these physiotherapy modalities with known metabolic, haemodynamic and respiratory effects may further exacerbate the similar effects of permissive hypercapnia and IRV, besides ARDS itself.

In contrast, two studies which included patients with ARDS among other diagnoses have shown beneficial effects of physiotherapy. Mackenzie and colleagues (1980), studying a sample of 42 ICU patients which included two patients with ARDS, found improved total lung/thorax compliance. This was supported by another study which also included two patients with ARDS in a cohort of 19 ICU patients (Mackenzie and Shin, 1985). In both studies, no control group was included. The clinical significance of these results is therefore questionable. If there are areas of recruitable collapsed alveoli, especially in the early acute stages (Gattinoni *et al*, 1994), and reduced mucociliary clearance in ARDS (Reynolds, 1987), then theoretically physiotherapy techniques could be of benefit. However, this remains to be determined.

Conclusion

The condition known as ARDS has been researched extensively over the past three decades since it was first described. There is consistent evidence of a multi-aetiological involvement of inflammatory cells and mediators, leading to inflammatory responses, membrane permeability and destruction of endothelial and epithelial lung cells. The mortality of ARDS remains high despite efforts in investigating the optimal therapeutic modalities. Recently, there has been a strong focus on body positioning as a supportive measure to improve arterial oxygenation, and thereby gas exchange, in these patients. The contribution of physiotherapy techniques in these patients remains speculative and awaits to be further investigated with regard to their potentially adverse or beneficial roles.

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