LUNG SQUEEZING TECHNIQUE AS A VOLUME RECRUITMENT MANOEUVRE IN CORRECTING LUNG ATELECTASIS FOR PRETERM INFANTS ON MECHANICAL VENTILATION

by

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Abstract:

The lung squeezing technique is derived from a theoretical model of modified forced expiratory technique and augmented tidal volume. It aims at promoting clearance of airway secretions and recruitment of the underventilated alveoli. Fifty-six preterm infants on mechanical ventilation presenting with lung atelectasis were enrolled in the study and were randomly assigned to 2 groups. Group A (n=26) was treated with a physiotherapy protocol using lung squeezing technique (LST) as a lung volume recruitment manoeuvre. Group B (n=30) received conventional physiotherapy using percussion and vibration technique on alternate side with the infant lying at the postural drainage position (PDPV). The outcome indicators were number of treatment sessions to attain re-opening of the collapsed lobes and recurrence rate of lung collapse within 3 days. The occurrence of adverse haemodynamic response during treatment was also compared. Eleven additional preterm infants without lung atelectasis were enrolled in a lung mechanics study, using the single breath occlusion technique. The changes in respiratory system compliance and resistance immediately and 4 hours after LST were investigated.

Measurement and Main Results:

LST was significantly more effective in correcting lung atelectasis for preterm infants on either conventional or high frequency oscillatory ventilation. After the first treatment session, 81% and 23% first re-expansion occurred in LST and PDPV group respectively ($p < 0.001$). This was also evident after stratification into IPPV mode ($p = 0.006$) and high frequency mode ($p = 0.006$). In lung mechanics study, respiratory system compliance improved by 21% ($p < 0.05$) and respiratory system resistance decreased by 26% ($p < 0.05$) immediately after LST. No major adverse effects were noted and there was no significant difference in haemodynamic disturbances when compared to PDPV.

Conclusion:

Lung Squeezing Technique (LST) is a safe, effective volume recruitment manoeuvre for correction of lung atelectasis. It is more effective than conventional PDPV in attaining re-expansion of the atelectatic segment, possibly by means of removal of airway secretions and alveoli recruitment.

肺壓技術對新生兒肺不張的療效

黃雅松

[摘要] **目的** 探討肺壓物理治療技術對新生兒肺不張的療效。 **方法** 採用隨機對照實驗方法，對 26 例肺不張及需用呼吸機新生兒用肺壓法治療，對照組 30 例用傳統叩擊，搖震法及姿式引流療法。 **結果** 以 X 線平片對兩組結果作了比較。肺壓法及傳統療法首次成功率分別爲 81% 及 23% ($p < 0.001$)。肺壓技術用於傳統呼吸機及高頻率呼吸機較傳統療法均有顯著療效 (p 值均 = 0.006)。兩組的血流動力紊亂並無分別。 **結論** 肺壓技術治療新生兒肺不張相比傳統療法效果較爲滿意，能提供有效的氣道排痰及肺泡擴張。

[關鍵詞] 肺壓技術　　物理治療　　新生兒肺不張

Table 1-1 List of abbreviations (in order of occurrence)

PD	Postural drainage
FET	Forced expiratory technique
FEV_1	Forced expiratory volume in 1 second
FVC	Forced vital capacity
PEFR	Peak expiratory flow rate
PIFR	Peak inspiratory flow rate
$\dot{V}_{max50}$	Maximum expiratory flow rate after exhaling 50% of vital capacity
EPP	Equal pressure point
HFV	High frequency ventilation
CPAP	Continuous positive airway pressure
IPPB	Intermittent positive pressure breathing
PEP	Positive expiratory pressure
PDPV	Postural drainage, percussion & vibration
PEA	Postextubation atelectasis
C_L	Lung compliance
C_W	Chest wall compliance
P_L	Lung recoil
V_L	Lung volume
HFO	High frequency oscillation
PaO_2	Arterial oxygen tension
$PaCO_2$	Arterial carbon dioxide tension
HMD	Hyaline membrane disease
PVH	Periventricular haemorrhage
ICP	Intracranial pressure
CT	Computerized tomography
MRI	Magnetic resonance imaging
$\dot{V}_{max}$	Maximal airflow
LST	Lung squeezing technique
MRB	Manual resuscitation bag
CXR	Chest radiograph
FiO_2	Fraction of inspiratory oxygen
IPPV	Intermittent positive pressure ventilation
IMV	Intermittent mandatory ventilation
HFOV	High frequency oscillatory ventilation
ODC	Oxygen dissociation curve
SaO_2	Oxygen saturation
ABG	Arterial blood gas
BPD	Bronchopulmonary dysplasia
IVH	Intra-ventricular haemorrhage
C_{rs}	Compliance of respiratory system
R_{rs}	Resistance of respiratory system
τ_{rs}	Time constant of respiratory system

Part I Introduction

1. Chapter 1 Background

With the advances in the management of very low birth weight neonates, lots of changes have been evolved in the past decades. The use of postnatal surfactant and prenatal steroids are effective to enhance fetal lung maturity (Halliday 1996), new modes of ventilation such as high frequency ventilation, nitric oxide therapy (Mupanemunda and Edwards 1995), nasal continuous positive airway pressure to facilitate extubation (Higgins et al.1991), which all direct new trends of management and clinical protocols in the neonatal intensive care settings.

The earliest published clinical study about neonatal chest physiotherapy was undertaken in 1969 (Holloway et al., cited by Bertone 1988). Research on physiotherapy for neonates can be summarised into several aspects:

1. Evaluation of the effects of specific treatment techniques like percussion, postural drainage (Finer and Boyd 1978), cupping and vibration (Tudehope and Bagley 1980)

2. The investigation of the physiologic changes during and after physiotherapy (Holloway et al, cited by Bertone 1988, Crane et al. 1978, Fox et al. 1978, Finer and Boyd 1978)

3. Estimation of the efficacy of physiotherapy in terms of amount of secretion removal (Etches and Scott 1978)

4. Evaluation of specific treatment protocols and their benefits to different patient populations, such as prevention of postextubation atelectasis (Finer et al. 1979)

There is controversy about the optimal modalities to be employed, primarily due to inappropriate application of chest physiotherapy or variations in research design. In most of the studies, there was difficulty in recruiting a homogeneous group of subjects or in enrolling sufficient sample size (Crane 1981). Many studies reported deterioration of physiological parameters after physiotherapy, but were not able to tell whether the

deterioration was caused by physiotherapy *per se* or by pharyngeal or endotracheal suctioning. Although percussion and vibration were the most commonly studied techniques, there were large variations in treatment regimens, and comparison of the efficacy of different techniques was difficult (Lewis et al. 1992).

1.1 Objectives

The objective of this study is to compare the lung squeezing technique, which is derived from a theoretical physiologic model, with the conventional physiotherapy in their efficacy in treating preterm infants with atelectasis of the lung. Reopening of the atelectatic lung demonstrated on chest radiograph is chosen as the primary outcome measure. Other outcome measures that reflect the efficacy, including recurrence of atelectasis, ventilation days, oxygen dependency days are also compared. Also evaluated are the physiological parameters that reflect the physiological disturbances caused by physiotherapy, including the pulse rate, blood pressure and oxygen saturation. Potential risks that might be contributed by physiotherapy are also investigated. The effects of the lung squeezing technique on lung mechanics are also studied.

1.2 Effects of chest physiotherapy

There are only few studies that evaluated the efficacy of chest physiotherapy in different types of specific lung diseases. The evaluation of the efficacy of different techniques of chest physiotherapy are even more scanty. After making a thorough review on chest physiotherapy, Sutton and colleagues (1982) concluded that postural drainage (PD) enhanced mucociliary clearance, PD with chest vibration and percussion improved pulmonary functions only in patients with large sputum volumes. In this review, most of the references were studies on cystic fibrosis, chronic bronchitis and asthmatic disease group. The value of physiotherapy on ventilation, gas exchange and work of breathing was not discussed. Mackenzie and colleagues (1978) reported that physiotherapy in adult ventilated patients did not improve PaO_2 despite a significant improvement in chest X-ray

appearance. An editorial review by Murray (1979) noted that improvement of pulmonary function after physiotherapy was only seen in patients with > 30 ml sputum cleared during treatment, indicating that PD with percussion and vibration modified pulmonary function mainly by removal of secretions. Although sputum clearance is a main aim in treating cystic fibrosis, Pryor and colleagues (1990) observed in cystic fibrosis patients only a marginal increase in SaO_2 during treatment with postural drainage using the active cycle of breathing techniques. In a meta-analysis of studies on chest physiotherapy in cystic fibrosis patients (Thomas et al. 1995), PD with percussion and vibration resulted in a significantly greater sputum expectoration than no treatment. Other treatment modalities, including forced expiratory technique, positive expiratory pressure mask, autogenic drainage and mechanical vibration, did not appear to have any therapeutic effect.

1.2.1 Aims of chest physiotherapy

The use of chest physiotherapy for patients with a variety of pulmonary problems is well entrenched in different medical care areas. Various manual techniques were developed like chest percussion, postural drainage, chest vibration, shaking, and forced expiratory technique. Murray (1979) commented that various components of chest physiotherapy were often introduced for one medical indication and then applied in other, sometimes dissimilar, medical conditions. Recently, more attention was paid to evaluating groups of patients with specific lung diseases to determine the efficacy of chest physiotherapy.

1.2.1.1 Mucus Removal

Postural drainage, percussion and vibratory-shaking

Postural drainage

Postural drainage (PD) is the utilisation of positioning appropriate to the site of lung pathology so as to allow gravity to assist the drainage of tracheobronchial secretions. Studies on the effect of PD alone are limited, although PD combined with other physiotherapy techniques have been shown to assist the clearance of tracheobronchial

secretions in conditions with copious bronchial secretions such as acute or chronic bronchitis, cystic fibrosis, and post-operative mucus retention (Bateman et al. 1979, Sutton et al. 1983, Webber et al 1986). Bateman and colleagues measured the clearance of bronchial secretion labelled with radioactive particles, and found that PD with percussion and vibration significantly increased clearance from different lung regions, especially from the central lung regions. Sutton and colleagues reported that sputum obtained by postural drainage combined with forced expiratory technique (FET & PD) was significantly greater than FET alone. Webber and colleagues also demonstrated a significant improvement in FEV_1, FVC, PEFR, PIFR and $\dot{V}_{max50}$ after treatment with postural drainage combined with forced expiratory technique, providing evidence that the technique could improve larger airway functions. This is further supported by Verboon and colleagues (1986), who demonstrated that sputum yielded with head-down tilt (-20°) drainage during sleep was significantly greater than the control group, when the technique was used on patients with copious sputum (>30g/24h).

Percussion, vibratory-shaking

Percussion is clapping the chest wall at approximately 5 Hz by hand or mechanical devices to produce an energy wave which is transmitted through the chest wall to the airways. The aim is to loosen secretions from bronchial walls. Clinically, the technique appears to be more effective when combined with deep breathing exercises. When used in neonates, the technique is modified by overlapping the second finger over the first and third so that percussion can be directed to a smaller area. Finer and Boyd (1978) introduced the technique of contact heel percussion using the thenar-hypothenar eminence of the hand for use in infants. The manoeuvre aimed at achieving a thoracic displacement of 1 to 2 cm at a frequency of 40 per minute.

Vibration (12-16 Hz) and shaking (2 Hz) involve intermittent chest wall compression applied during expiration, and are believed to have a similar effect in loosening secretions in the airways as percussion. Etches and Scott (1978) measured and compared the amount of secretions removed with or without physiotherapy in six infants with "secretion

problem" in the respiratory tract. The mean weight of secretions removed after physiotherapy was greater than that removed by suction alone. The result however is not conclusive due to the small sample size.

By measuring the clearance of excessive bronchial secretion labelled with radioactive particles, Bateman and colleagues (1979) reported favourable effect of PD used in combination with percussion and vibration on bronchial clearance, but there was no differentiation of which component was contributing to this effect or whether this was a combined effect. Objective assessment of the efficacy of physiotherapy in tracheobronchial clearance in adult patients with mucus hypersecretion was also reported by Sutton et al. (1985). There was no evidence that postural drainage combined with percussion, and vibratory-shaking increased tracheobronchial clearance of either radioaerosol or labelled secretions (sputum-specific radioactivity) when compared to PD alone. However, the wet weight of sputum removed was significantly increased when PD, percussion, and vibratory-shaking were used in conjunction with deep breathing. It appears that deep breathing had contributed to this increase in sputum removal.

The exact mechanism of action of percussion and vibration is still not clear, although it is assumed that percussion and vibration augment the effect of gravity on bronchial clearance, when the patient is in the postural drainage positions (Imle 1989).

Airflow acceleration manoeuvres

Forced expiratory technique

Breathing exercises aim to increase ventilation above normal tidal breathing and may enhance mucus clearance as described, although little is reported about their effect on regional ventilation. Other modified techniques like forced expiratory technique (FET) were developed and reported to be effective when used alone or in combination with postural drainage in assisting sputum removal and aerosol clearance (Sutton et al. 1983). Webber and colleagues (1986) also demonstrated that FET used with PD could improve large airway function in cystic fibrosis patients as evidenced by a significant improvement in FEV_1, FVC, PEFR, PIFR and $\dot{V}_{max50}$, following their use. Hasani and colleagues (1991) further investigated the effect of FET on regional clearance of inhaled radioaerosol in seven patients with airway obstruction. Patients receiving FET had more clearance of lung radioactivity than the control group, although statistical significance was not attained.

FET mobilises bronchial secretions by generating a high rate of airflow in the compressed airways by means of huffs from mid-lung volume to low-lung volume (Selsby and Jones 1990). Dynamic compression of the airways with the narrowed segment moving rapidly past the carina upstream into the small bronchi can be visualised in cine tracheobronchogram, as the lung volume diminishes during a cough. FET promotes mucus clearance in this compressed lumen by creating a very high gas velocity which facilitates mucus detachment from the wall of airways, as long as these airways remain patent.

There is little research done on airflow acceleration techniques in patients who are on mechanical ventilators, especially in the neonatal population. Dynamic compression of small collapsible airways during forced expiration plays an important role in the airflow acceleration techniques (Colbert 1993a). During forced expiration, there is some point along the airways where the intrabronchial pressure is equal to the extrabronhcial pressure, named as equal pressure point (EPP). As lung volume diminishes, this EPP moves from the larger to the smaller airways, resulting in collapse of the small bronchioles which are

not supported by cartilage. As lung volume diminishes further, more and more smaller bronchioles are exposed to potentially collapsing pressure. Zapletal and colleagues (1983) also suggested that the immediate deterioration in ventilation after chest physiotherapy in a group of cystic fibrosis patients were caused by collapse of the central airways, as demonstrated in cinebronchographic studies. The narrowing of the trachea and bronchi, and collapse of the larger bronchi might impair mucus clearance from the peripheral airways. The physiotherapy regimen in Zapletal's study consisted of percussion and vibration with postural drainage. Repeated vigorous coughing following these manoeuvres was thought to be the cause for central airway collapse and deterioration of the ventilatory parameters.

Other studies on mucociliary function of the airways during high frequency ventilation (HFV) have yielded conflicting results. This aspect will be discussed in the section on HFV.

Positive expiratory pressure therapy

Devices used to generate a positive expiratory airway pressure include continuous positive airway pressure (CPAP), intermittent positive pressure breathing (IPPB), PEP mask, flutter VRP1 and TheraPEP. By expiring against an external airflow obstruction, a positive expiratory airway pressure is created which theoretically helps to dilate airways up to the peripheral bronchioles, even the intrapulmonary distribution of ventilation, and open up atelectatic regions (Groth et al. 1985), thereby improving mucus removal (Falk et al. 1984, Tønnesen and Støvring 1984). Falk and colleagues reported that in patients with cystic fibrosis, PEP combined with postural drainage (PD & PEP) was more effective than forced expiratory technique (FET) or PD combined with percussion and vibration (PDPV) in bringing about sputum expectoration. This finding was supported by a study on chronic bronchitis patients in whom the use of PEP mask with FET was found to be superior to FET alone in lessening respiratory symptoms and the number of acute exacerbations, although there was no significant change in lung function parameters (Christensen et al 1990). Sutton et al. (1982) suggested that PEP might enhance the effect of forced

expiration by moving the equal pressure point of dynamic compression peripherally, thereby assisting the removal of mucus from the smaller bronchi.

1.2.1.2 Re-expansion of atelectatic lung

In the adult lung, the presence of collateral ventilation and trapped nitrogen are important in keeping the lobe inflated when the lobar bronchiole is obstructed. In excised adult human lung, it has been shown that positive end expiratory pressure re-expands a collapsed lobe during mechanical ventilation, by working through both the ordinary bronchial route and the collateral channels (Andersen et al. 1979). In neonates, the lack of collateral ventilation may be an important factor to the pathogenesis of lobar collapse. Other factors may include the smaller and more collapsible airways, high chest wall compliance, increased elastic recoil resulting from surfactant deficiency, and insufficient inspiratory force (Redding 1984).

In preterm infants, lobar collapse during mechanical ventilation and postextubation atelectasis (PEA) are common indications for chest physiotherapy. Finer and colleagues (1979) reported an incidence of 38% (8 out of 21) of PEA in preterm infants without physiotherapy, and none in all 21 infants who were treated with a five minutes vibration physiotherapy regimen, the development of PEA had resulted in a high rate of re-intubation. Higgins et al. (1991) have reported that the use of nasal CPAP can further facilitate successful extubation, especially in neonates less than 1000 g. Nasal CPAP probably works by stenting the upper airway and preventing obstructive apnoea. Wyman and Kuhns (1977) also reported that postextubation atelectasis was associated with a high rate of re-intubation (7 out of 11) in ventilated infants and suggested that prophylactic physiotherapy may be beneficial.

Conducting airway plugging may also be caused by necrotic epithelium admixed with mucus. Metlay and colleagues (1983) reported a lesion in ventilated newborns, named necrotizing tracheobronchitis, which is characterised by the presence of diffuse coagulative necrosis of the epithelium in the trachea and the main bronchi. Nagaraj and colleagues

(1980) also reported that recurrent lobar atelectasis might be caused by acquired bronchial stenosis resulting from the healing process of coagulative tracheobronchial necrosis. In this report, acquired bronchial stenosis or obstruction by granulation tissue causing atelectasis was observed in ten infants requiring mechanical ventilation and frequent suctioning. These infants did not respond to a physiotherapy regimen of chest vibration and postural drainage, and required bronchoscopic aspiration or excision and cauterisation of the granulation tissue.

In ventilated subjects, when part of the lung is collapsed, the remaining patent lung segment will receive the entire tidal breath and become over-distended, and less compliant. The distension will also lead to barotrauma, especially in an immature lung, or pneumothorax when the over-distended alveoli are ruptured (Grosfeld et al. 1980). Gas exchange abnormalities associated with atelectasis are partly compensated by a local pulmonary vasoconstriction response, which directs blood to the ventilated areas. However, this mechanism is impaired if a large area of atelectasis is present , or when the lung is ventilated with a high positive end expiratory pressure (Redding 1984). A study using respiratory mass spectrometer (Morrell et al. 1995) also supported that ventilation-perfusion balance in the presence of airway obstruction depends not only on this hypoxic pulmonary vasoconstriction beyond obstructed airways, but also the matching of redistributed blood flow and ventilation to the rest of the lung. Severe pulmonary atelectasis may result in severe respiratory failure with hypoxaemia due to ventilation-perfusion mismatch.

1.2.2 Chest physiotherapy for neonates

1.2.2.1 Pulmonary characteristics in neonates

The immature lung (19-20 wk gestation) has smooth-wall respiratory channels lined by cuboidal epithelium. Further development of acinus occurs between 22 and 24 wk gestation. After 28 wk gestation, there is a marked decrease in the prominence of the interstitial tissue, and the saccular walls become more narrower and more compact.

Increase in conducting airway proportion is significant at this stage. Acquisition of alveoli may occur as early as 30 to 32 wk gestation. True respiratory bronchioles appear later after late gestation and early neonatal period (Langston et al. 1984).

Similar angles of tracheal bifurcation are noted in the neonate when compared to adults, with 24° for the right and 44° for the left (Fewell et al. 1979). In the neonatal period, the respiratory zone of the lung is composed of three generations of respiratory bronchioles and one order of alveolar ducts and sacs, increasing to four generations of respiratory bronchioles and three orders of alveolar ducts and sacs by two months of age (Wailoo and Emery 1982). Collateral ventilation is deficient at birth, as the pores of Kohn and channels of Lambert develop only at one and six years of age respectively (Menkes and Traystmen 1977). This lack of collateral ventilation channels means that alveolar opening in infants have to be maintained solely through the alveolar ducts, and any airway occlusion will result in atelectasis.

Structurally, the diameter of the alveolus is about 75μ in preterm infants, about ¾ of the size in term infants. The diameters of the alveolar ducts and respiratory bronchioles are also relatively small. Lung air volume and lung recoil (P_L) are low due to low pulmonary elastin and collagen content. This plastic behaviour of the neonatal lung tissue may cause a decrease in lung compliance (C_L), especially during expiration. In the newborn, the chest wall compliance (C_W) is about five times the lung compliance (C_L). The compliant chest cage contributes to an inefficient respiratory mechanics: during inspiration, a significant proportion of potentially inspired volume is lost due to paradoxical chest wall distortion such as sternal recession and subcostal insucking. At end expiration, the flexible chest cage also causes the resting lung volume (V_L) to approach the residual volume as a result of a high $C_W \div C_L$ ratio (Mortola 1994). The highly compliant chest wall also increases the tendency of the small peripheral airways to close during tidal breathing, and increases the likelihood of airway obstruction (Dezateux and Stocks 1997).

Thus the immature lungs of preterm infants are characterised by three interrelated factors: small respiratory units, frail chest cage, and surfactant deficiency. All three factors contribute to a tendency to develop atelectasis (Tooley et al. 1973).

Alveolar opening, which must take place to allow gas exchange, is regulated by two forces: (1) The driving force between the conducting airway and the alveoli (2) The recoil forces of the lung and chest wall. According to Laplace's Law*, if the lungs were composed of interconnected alveoli of different sizes, there is always a tendency for the smaller alveoli emptying into the larger ones. The collapsed alveoli will require very large distending pressures to reopen, because of the cohesive forces at the liquid-liquid interface of collapsed alveoli. Pulmonary surfactant stabilises the lung by reducing the surface tension at the air-liquid interface of the alveoli, particularly during expiration (Schurch et al. 1995). In preterm infants, surfactant deficiency and dysfunction are the most important contributing factors to the pathogenesis of respiratory distress syndrome.

1.2.3 Chest physiotherapy for infants on mechanical ventilation

1.2.3.1 Conventional ventilation

Studies (Javorka et al. 1982) on mechanics of breathing during sneezing and crying in premature newborns showed that ventilation increased considerably in crying when compared with quiet breathing. This may be due to the recruitment of the inactive alveoli. In the expulsive phase of sneezing, a peak expiratory airflow 6.6 times higher than the flow during quiet breathing is generated. This is produced by a high intrathoracic pressure (about 4.8 times of adult), which is thought to be an adaptation to eliminate noxious substances through the smaller lumens of the premature infants. Both mechanisms may help to prevent the development of atelectasis. For premature infants who require artificial ventilation, it is evident that both mechanisms are abolished due to the presence of an

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* Laplace's law, P=2ST/r, where :
P = the force required to maintain a respiratory unit of radius r
r = the radius of the respiratory unit
ST = surface tension at interface between intrapulmonary gas and lining of respiratory units

endotracheal tube, although no study has looked into the relation of artificial ventilation and incidence of atelectasis.

Touw and colleagues (1993) investigated the consequences of expiratory chest wall compression in a mechanically ventilated canine model of severe pulmonary hyperinflation. End expiratory lung volume and cardiac output were both decreased by manual rib cage compression during expiration. A significant increase in mean pleural pressure and mean expiratory pleural pressure observed during the procedure might have contributed to the reduction in cardiac output. Although this animal study was performed on a severe pulmonary hyperinflation model, similar changes might occur in ventilated infants since lung hyperinflation may be present during mechanical ventilation and the compression manoeuvre is similar to the lung squeezing technique in some aspects.

1.2.3.2 High frequency ventilation

High frequency ventilation (HFV) has been used to treat neonatal respiratory distress for the past decade. Early intervention with a lung recruitment strategy after surfactant replacement has resulted in a reduction in both acute and chronic lung injury. Although a meta-analysis of 12 randomised clinical trials (Gerstmann et al. 1996) showed that high frequency ventilation made no difference in mortality when compared to conventional ventilation, high frequency ventilation might still be a beneficial intervention as there was an improvement in survival without chronic lung disease.

One common belief is that the oscillations of the airways created by the ventilator might be useful in mobilising the secretions inside the airways, thus promoting mucus removal. The other belief is that as long as the lung is being ventilated in a optimal volume, alveolar opening will be maximal and the chance of segmental lung collapse is low. However, the results of animal studies are not conclusive. McEvoy and colleagues (1982) showed that high frequency oscillation (HFO) inhibited lung mucociliary clearance, and even caused retrograde movement of secretion from the trachea into the more distal airways, and

accumulating preferentially in the middle region of the lung. The pooling of mucus might occlude the smaller bronchi, thus causing segmental or lobar atelectasis.

Retrograde movement or depressed clearance of secretion during HFO was however not found in other studies. A striking finding in the study by King et al. (1984) was the enhancement of mucus clearance (tracheal mucus clearance rate) by high frequency oscillation delivered externally around the chest wall, with a clearance rate 2.4 times of the spontaneously breathing controls. This increase in mucus clearance rate might be due to a cephalad bias in airflow and a greater peak expiratory air flow when compared to inspiratory airflow.

The effect of forced expiratory manoeuvre on airway collapse and the consequent flow mechanism during high frequency ventilation is still poorly understood. According to the computational and experimental models of high frequency oscillation by Pedley and colleagues (1994), dynamic airway collapse and flow limiting phenomenon might occur during a forced vital capacity manoeuvre.

Another area of concern is the effect of humidification on mucociliary transport. Inadequate humidification of insufflated gases, which occurs easily during HFV because of high gas flow rates involved, can seriously impair mucus transport in the airway (Wetzel and Gioia 1987).

2. Chapter 2 Neonatal Chest Physiotherapy

2.1 Traditional physiotherapy means

2.1.1 Percussion and Chest vibration

Finer and Boyd (1978) evaluated the effect of percussion on 20 neonates and showed that postural drainage with percussion for 20 minutes produced significant increase in PaO_2. Tudehope and Bagley (1980) compared three physiotherapy techniques on 15 newborn infants on assisted ventilation: contact heel percussion, cupping with Bennett face mask and electric toothbrush vibration. Each treatment was combined with 4 drainage positions for a total of twelve minutes, followed by suctioning. Post treatment increase in oxygenation (PaO_2) was observed in the percussion and cupping group with no significant changes in $PaCO_2$ or pH.

Duara and colleagues (1983) compared different percussion time intervals (0.5, 1.5, and 2.5 min) and showed that percussion for 2.5 min produced the greatest improvement in lung compliance (C_L) and inspiratory and expiratory resistance without any cardiovascular compromise. The sample size of this study is small, with only six intubated infants enrolled.

Chest vibration is usually delivered to neonates in conjunction with postural drainage and percussion. The technique of vibration consisted of using two or three fingers to deliver anteroposterior oscillatory movements through direct contact with the chest wall. Finer and colleagues (1979) conducted a retrospective review and a prospective controlled study on 85 neonates to evaluate the effect of physiotherapy on prevention of postextubation atelectasis. Chest vibration with postural drainage, performed for a minimum of five minutes hourly on first day after extubation, significantly reduced the incidence of postextubation atelectasis when compared to postural drainage alone. The occurrence of postextubation atelectasis was thought to be the result of retained secretions and mucosal oedema.

Eckmann and colleagues (1996) showed that low amplitude (0.2 cm) and high frequency (15-30 Hz) chest vibration delivered by a motor redistributed intra-airway CO_2 during tracheal insufflation in dogs receiving intermittent positive pressure ventilation for ventilatory failure. Gas exchange was improved by intraluminal mixing, with an enhancement of CO_2 transport from the periphery of the lung to the mouth. There is however no evidence that manual chest vibration delivered by physiotherapists gives a similar effect.

2.1.2 Cup percussion (Cupping)

Percussion to neonates may also be delivered by using various cup-shaped objects, such as the Bennett face mask (Parker 1985, Bertone 1988). The efficacy and physiological changes in infants during cupping with the Bennett face mask have been investigated by previous workers (Tudehope and Bagley 1980, Peters, cited by Lewis 1992). Compared to contact heel percussion, cupping was less well tolerated and was associated with greater adverse physiological changes, including increase in heart rate, respiratory rate and activity levels. Despite these findings, cupping is extensively used in some neonatal centres according to a survey of Australian neonatal intensive care units (Lewis 1992). In 1994, this physiotherapy technique was banned in Auckland (reported by Coney 1995), suspecting that cupping may result in dangerous fluctuations in cerebral blood flow and associated brain damage in low birth weight infants. The concern will be further discussed in the section of cystic brain lesions.

2.1.3 Postural drainage (PD)

Crane and colleagues (1978) measured changes of arterial blood gases, heart rate, respiratory rate, blood pressure and transcutaneous O_2 during physiotherapy in 24 infants with hyaline membrane disease. Percussion and vibration were combined with drainage with head tilt to form four different groups for comparison. All physiological parameters increased in all four groups. However, significantly higher systolic pressure was recorded in the group treated in head-down position.

According to Finer and Boyd (1978), postural drainage alone did not improve PaO_2 since the small calibre of the airways of premature infants may not allow secretions to drain just by the effect of gravitational force. However, Wagaman and colleagues (1979) investigated the effect of different positioning on lung mechanics and arterial oxygen tension in a group of intubated infants. PaO_2 and lung compliance significantly increased when the infant was in the prone positioning. This might be attributed to better diaphragmatic excursion and improved ventilation to perfusion ratio due to less alveolar collapse within the lung.

Although the effect of postural drainage for infants is inconclusive, significant improvement of PaO_2 was observed when PD was combined with percussion in the study by Finer and Boyd. Finer and colleagues (1979) also reported that chest vibration, when combined with postural drainage significantly reduced the incidence of postextubation atelectasis in infants.

2.1.4 Endotracheal Suctioning

The use of chest physiotherapy, in combination with tracheobronchial suctioning have been shown to be effective in treating atelectasis in ventilated infants and in preventing mucus plugging of endotracheal tubes of small diameter. Using angulated catheter together with head turning for selective bronchial suctioning, can be carried out to treat lobar atelectasis or atelectasis of the left lung (Placzek and Silverman 1983). Lung mechanics studies in intubated preterm infants after tracheobronchial suctioning have also showed significant fall in airway resistance and time constant (Prendiville et al.1986).

2.1.4.1 Adverse effects of endotracheal suctioning

Deep endotracheal or tracheobronchial suctioning requires the introduction of the suction catheter into the airway through the endotracheal tube until resistance is met, when the catheter tip is impacted at the carina or a small-diameter bronchus. The catheter is then withdrawn slightly followed by continuous application of suction pressure and slow

withdrawal of the catheter until it is completely removed from the endotracheal tube. Severe tissue injuries including disruption and inflammation of mucosa, near total loss of cilia, and necrotic changes in bronchi and carina after series of deep suctioning have been reported in animal studies (Bailey et al. 1988). In these studies, however the suctioning frequency (every 15 minutes for 6 hours) was much greater than that practised in clinical situation. The studies also did not compare the effectiveness of mucus removal between deep and shallow suction. Other complications of deep endotracheal suctioning including pneumothorax had also been reported (Vaughan et al. 1978).

Given the inconclusive evidence, physiotherapists attempting to clear the secretion in an infant's carina region have to judge whether to use a deep or shallow suctioning protocol after chest physiotherapy based on the infant's clinical condition. When deep suctioning were to be used, the frequency should be kept to a minimum, and additional caution should be exercised in introducing the suction catheter beyond the tip of endotracheal tube, so that the possible hazards of deep suctioning can be minimised. As stated by Runton (1992) after reviewing a large series of suctioning policies and techniques, suctioning an artificial airway is a procedure requiring great assessment skills, and suctioning can cause extensive damage when the suction catheter is advanced too far.

Endotracheal suctioning has been associated with a number of adverse effects, including bradycardia, oxygen desaturation, increase in blood pressure and post suctioning hypotension (Simbruner 1981). These effects may be attributed to the following factors:

- Disconnection of the endotracheal tube resulting in a loss of ventilatory support pressure and supplemental oxygen
- Removal of the gas inside the proximal airways
- Stimulation of the trachea

Fox and colleagues (1978) investigated the physiologic alterations in respiratory function associated with chest physiotherapy and endotracheal suctioning in intubated infants. There was a significant drop in mean PaO_2 (30 torr) immediately after vibration of the chest using a portable vibrator and suctioning of the airway. The hypoxaemia was not

caused by lung atelectasis, and was associated with a decrease in inspiratory and expiratory resistance which indicated that mucus obstructing the airways had been successfully removed. Since the vibration duration is extremely short (30 sec), it is likely that hypoxaemia was mainly caused by the endotracheal suctioning. Neonates with hyaline membrane disease (HMD) particularly respond adversely to endotracheal suctioning with desaturation and bradycardia, which can be minimised by the use of supplemental oxygen at 20% higher than the maintenance FiO_2 and hyperventilation (Cunningham et al. 1983, Tudehop and Bagley 1980).

Atelectasis following tracheal suction in infants has been reported by Brandstater and Muallem (1969). The extent of atelectasis, as represented by compliance change and the subsequent behaviour of the collapsed areas, was increased when suctioning was prolonged or when a large suction catheter was used in a small endotracheal tube (e.g. a No. 8 French size suction catheter with a 3 mm endotracheal tube). Collapse of the right upper lobe is particularly common after endotracheal suctioning, being present in 34 of 102 ventilated infants in one study (Boothroyd et al. 1996). Possible causes include:

- Selective intubation of the right bronchus
- "Over-vigorous" uncontrolled endotracheal suction selectively emptying the RUL
- Trauma causing oedema at the RUL bronchial orifice

Other studies also reported that there was an increase in intracranial pressure during endotracheal suctioning in brain injury children. This pressure increase can be attributed to tracheal stimulation, rather than an increase in the $PaCO_2$ after suctioning (Fisher et al. 1982). Shah and colleagues (1992) investigated this phenomenon further in preterm infants (n=12) and observed the following sequence of changes:

- Desaturation in the arterial and cerebral circulations began within 5 seconds of the onset of suctioning
- Cerebral deoxygenation
- Cerebral blood volume increased during suction

- Arterial reoxygenation began with the onset of reventilation
- Reoxygenation in the brain was delayed by 15 seconds

2.2 Possible Complications of chest physiotherapy

In intubated newborn infants, chest physiotherapy is commonly used as part the airway management. However, there are only few available data on the specific physiologic effects of these procedures.

2.2.1 Haemodynamic disturbances

Haemodynamic disturbances in preterm infants are common during motor activities, routine handling, seizures and apnoea. Since the auto-regulation of cerebral blood flow is impaired in these infants especially in the first 3-4 days of life, fluctuation in arterial blood pressure is thought to be a main factor in the development of haemorrhage in the germinal matrix (Lou et al.1979). Lou and colleagues reported that 40% of premature neonates (birth-weight < 1500 g) had cerebral bleeds in the first 3 or 4 days of extra-uterine life. Volpe (1992) also reported that in the survivors of infant ≤ 1500 g body weight, 5-15% exhibited major spastic deficits and another 25-50% exhibited developmental disabilities, as manifestations of perinatal brain injury. D'Souza and colleagues (1995) investigated the association of blood pressure, heart rate, skin temperature to periventricular haemorrhage (PVH) in preterm infants and suggested that blood pressure instability in infants were affected by gestation. Minimal handling , prevention of epileptic seizure and apnoea, control of blood pressure by drugs had been suggested as possible means for the prevention of PVH.

Most studies demonstrated that currently accepted methods of chest physiotherapy were not without potential serious side effects in neonates. Tachycardia, tachypnea, and increase in systolic pressure were commonly caused by the procedures (Crane et al. 1978). Postural drainage with head tilt also resulted in arterial hypertension. Chen et al. (1995) have demonstrated in term neonates that there was a trend for systolic and diastolic blood

pressure to increase in the head down position (-30°), although this increase was not statistically significant when compared to the blood pressure at the head up (30°) and supine position. Ross and colleagues (1992) studied the effect of PD at different positions in healthy subjects and reported that distribution of ventilation was significantly less homogeneous in the side-lying positions compared to the supine and sitting positions. These results reflect a position-induced change in pleural pressure gradient, and also intraregional changes in ventilation distribution. These effect on ventilation homogeneity may predispose a patient to arterial desaturation.

A drop in PaO_2 after endotracheal suctioning has also been reported by Fox et al. (1978), who suggested that the hypoxaemia was most likely caused by increased R to L shunting, secondary to elevated oesophageal pressures (intrapleural pressure) in agitated infants.

2.2.2 Fluctuation of Cerebral Perfusion

Pressure autoregulation mechanism is responsible for the maintenance of a constant cerebral blood flow within a wide range of arterial blood pressure. Little is known about the development of this mechanism in newborn infant (Pryds and Edwards 1996). Fanconi and Duc (1987) reported that non-paralysed ventilated infants had a significantly larger increase of intracranial pressure (ICP) and reduction in cerebral perfusion pressure during intratracheal suctioning, when compared to the paralysed ones. There is evidence that struggling , coughing, and asynchronised breathing may cause an acute congestion of the cerebral veins by impediment of cerebral venous return, which results in spiking intracranial pressure, decrease in cerebral perfusion pressure, and changes in cerebral blood flow. All these changes may be related to the pathogenesis of intracranial hemorrhage in preterm infants.

Most of the studies evaluating the cerebral effects of physiotherapy was however not able to differentiate the physiologic disturbances from physiotherapy *per se* and those caused by tracheal suctioning.

2.2.3 Cystic brain lesions

Harding (1994) speculated that certain technique (cup percussion) of physiotherapy might be related to the development of postnatal encephaloclastic porencephaly (Coney 1995). This distinctive pattern of severe brain injury was first reported by Cross and colleagues (1992) in 15 very low birth weight neonates (<1500 g), who also described the evolution of its ultrasound changes as dense peripheral lesions initially, progressing to mixed dense and cystic lesions, and finally gross cystic lesions with medial sparing. The median age of the three phases of evolution was 16, 22 and 28 days respectively. The exact aetiology of this lesion remains obscure. It is suspected to be related to cup percussion because of its similarity to the brain injury in older children caused by violent shaking, which causes head movement similar to that observed during cup percussion. However, other common clinical features of the shaken baby syndrome, such as retinal haemorrhage, and subdural hematoma were not observed in either Harding's or Cross's report. The pathogenesis of cystic brain lesions in preterm infants may be a progression of severe periventricular leukomalacia (Volpe 1992, 1996), a non-haemorrhagic lesion caused by systemic hypotension and impaired cerebral blood flow. Single, asymmetric, large and persistent cyst formation may also develop in periventricular haemorrhagic infarction.

Repetitive shaking of the head also occurs in preterm infants on high frequency oscillatory ventilation. A meta-analysis of 12 randomised clinical trials on high frequency ventilation did not show any difference in the occurrence of periventricular leukomalacia when compared to infants on conventional ventilation (Gerstmann et al. 1996).

Based on the above information, it is likely that changes of physiologic parameters, such as PaO_2, ICP, cerebral perfusion pressure can occur in any agitated infants. An infant can become agitated during endotracheal suctioning, or any kind of vigorous physiotherapy manoeuvres. With the advent of near-infrared spectroscopy, continuous measurement of in vivo cerebral oxygenation and hemodynamic changes has now become possible, and may provide more information on the relationship between chest physiotherapy and intracerebral complication in the high risk infants (Plessis 1995).

2.3 Modified manual techniques

Macdonald (1972) categorised physiotherapeutic methods into three types: (1) Postural drainage, percussion and suction are useful to clear secretion and debris form the bronchial tree (2) Vibrations, rib-springing and posturing assist thoracic movement (3) Periodic position changing relieves pulmonary congestion. There are extensive studies on percussion, vibration, postural drainage and suctioning. However, we are not aware of any detailed description or research on the use of rib-springing or other similar forms of manoeuvre in the neonatal population.

2.3.1 Theoretical model of lung squeezing technique

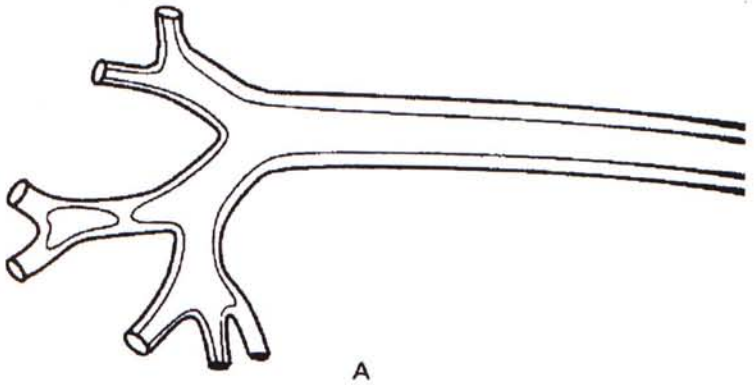
The underlying mechanism of physiotherapy in opening atelectatic lung segment is still not clearly understood. According to Mackenzie and colleagues (1989), there are at least four known contributing factors: (1) Increase in transpulmonary pressure by deep breathing and rib-springing at the end of expiration (2) Positioning of atelectatic segment non-dependently in the optimal position for gravity to assist in bronchial drainage (3) Generation of pressure differences between atelectatic segment and open airways by means of cough, huffing or forced expiratory technique (4) Interdependence of lung parenchyma to assist in the reexpansion of the atelectatic areas by the surrounding normally ventilated areas.

Based on previous studies, postural drainage may not effective in neonates as compared to adult subjects due to the small calibre of the airways. There is also the concern that PD might disturb ventilation homogeneity and physiological functions in the small infants. The factor of lung parenchymal interdependence may be of little effect on atelectasis re-expansion due to low lung recoil in neonates.

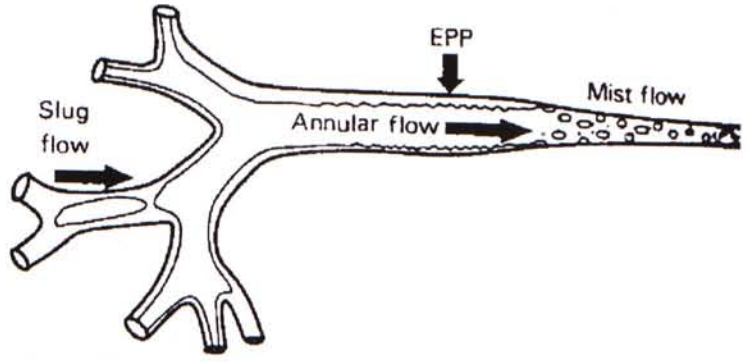
In contrast, forced expiratory technique is effective in clearance of bronchial secretions and provides an augmentation of airflow inside the bronchial tree during expiration. During FET, compression of airways occurs downstream (towards the mouth) of the end

pressure point. EPP, first described by Mead and colleagues, is a point along the airway where the intrabronchial pressure is equal to the extrabronchial pressure (Light 1995). Selsby and Jones (1990) used a cine tracheobronchogram, and visualised that this dynamically compressed segment moves rapidly unpstream past the carina into the small bronchi as the lung volume decreases during a cough. High gas velocity is produced at the compressed segment which gives mist flow and promote mucus detachment (Figure. 2.1).

Figure 2-1: Diagram showing action of forced expiratory technique (FET)



A



B

A: Airways lined with mucus layer. B: During forced expiration, high gas velocity occurs at the narrowed segment which causes mucus detachment. EPP = equal pressure point, a point along airway where intrabronchial pressure equals to extrabronchial pressure. During forced expiration, EPP moves upstream ahead of the narrowed downstream segment (After Selsby and Jones 1990)

Air trapping may occur if excessive pressure is exerted on a long segment of collapsible or unsupported bronchioles resulting in its closure. This occurs particularly commonly in preterm infants receiving FET because of their small and easily collapsible bronchioles and highly compliant chest wall. Airways beyond generation 11, which include the bronchioles, terminal bronchioles and respiratory bronchioles, have no structural support and their patency rely on traction force arising from the elastic recoil of the lung tissues (Nunn 1987). As demonstrated by Light (1995), the maximal flow ($\dot{V}_{max}$) in the airways is governed by (1) the elastic recoil of the lung ($Pst_{(L)}$), (2) tendency of the airways to collapse (Ptm') and, (3) resistance of the upstream segment (Rs):

$$\dot{V}_{max} = \frac{Pst_{(L)} - Ptm'}{Rs}$$

Air trapping will occurs when $Pst_{(L)}$ is less than Ptm' , rendering zero flow ($\dot{V}_{max} = 0$) in the airway. During any kind of chest compression manoeuvres, there is always a tendency for the Ptm' to increase and exceed $Pst_{(L)}$, thus resulting in air trapping. This is extremely likely to occur in preterm infants due to small size of the airways and low lung recoil.

In order to avoid the occurrence of excessive dynamic compression or closure of the small collapsible airways, we use a lung squeezing technique (LST) with moderate force (F_{LST}) to give gentle compression which allows generation of optimal expiratory flow rate (Figure 2.2). Based on the pulmonary flow-volume curves, when too little compression force (i.e. less than F_{LST}) is used, optimal expiratory flow rate will not be reached. According to Alison and Ellis (1992), the expiratory flow rate cannot be altered at mid or low lung volume, no matter how great the expiratory effort is made, meaning that flow is independent of maximal effort at the expiratory reserve range as long as compression force is greater than F_{LST}. However, in order to avoid excessive airway compression and closure, excessive force greater than the F_{LST} is avoided.

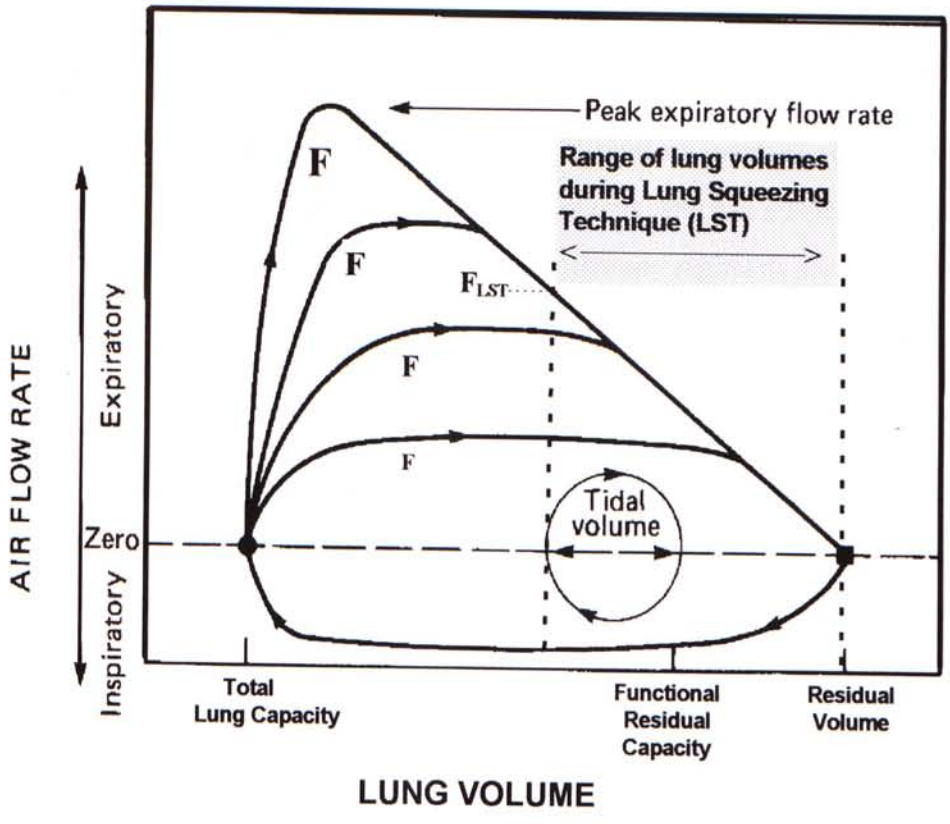


Figure 2-2: Flow-volume curves showing optimal expiratory flow rate during lung squeezing technique (LST)

Flow-volume curves at four levels of expiratory effort (F) (letter size denotes different levels of effort). Within limits, peak expiratory flow rate is dependent on effort but, during the latter part of expiration, at mid to low lung volumes, all curves fall on an effort-independent section where flow rate is limited by airway collapse. Lung Squeezing technique (LST) works in range of expiratory reserve volume, and coincides with majority of the effort independent section

F_{LST}: Chest compression force used during LST to generate optimal expiratory flow rate, without risk of excessive dynamic compression or closure of small collapsible airways (Modified from Nunn JF: Applied Respiratory Physiology 3rd ed Butterworths 1987, p.61.)

Since the lung squeezing is delivered in the range of expiratory reserve volume of a specific thoracic region, or the effort independent portion of the flow-volume curve, the flow rate achieved to mobilise secretion should be reaching maximum as long as a compression force equal to or slightly greater than F_{LST} is being used. These enhanced tidal breaths in the range of expiratory reserve volume is used to loosen mucus from peripheral airways. Similar rationale utilising unforced expiratory manoeuvre is practised in autogenic drainage to achieve peripheral loosening of mucus, and has a better result in sputum mobilisation when compared to other physiotherapy regimens such as PEP, postural drainage and conventional physiotherapy (McIlwaine et al. 1988, cited by David 1991).

In order to incorporate the effect of increase transpulmonary pressure on mucus loosening, the manoeuvre also takes advantage of the compliant chest wall of the preterm infants. After three or four graded successive chest wall compressions, that part of thoracic region is compressed to almost full expiration position. This is followed by a quick release of the compression pressure to allow the reexpansion of that thoracic segment.

During the course of deep breathing, initial work is used in opening up alveoli and the smallest bronchioles. The initial part of the inflation limb on volume-pressure curves (Figure 2.3) is almost flat until the critical opening pressure of the alveoli and bronchioles is exceeded (Point X_1). In the later part of the inflation limb, work is used to stretch the elastic components within the system with much more ease (Colbert 1993b). The use of quick release is intended to generate a marked increase in transpulmonary pressure at the initial part of lung inflation, so as to facilitate opening of the alveoli and small airways. During the deflation process, volume changes lag behind pressure changes much more than during inflation, meaning that less pressure is needed to keep the alveoli patent than to open them.

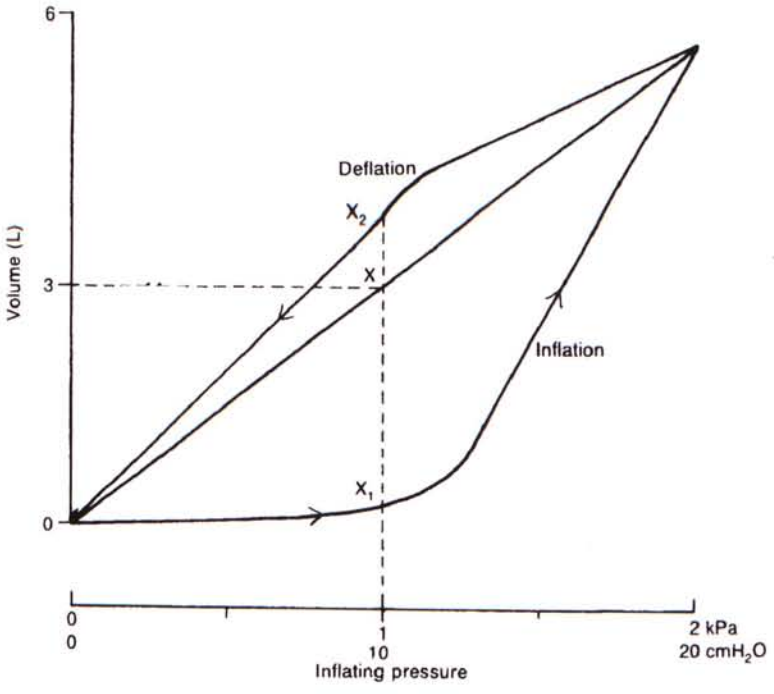


Figure 2-3: Volume-pressure curves from fully deflation to fully inflation of the lungs

Lung inflation occurs after point X_1, which denotes critical opening pressure of alveoli and bronchioles (Modified from Colbert D. Fundamentals of clinical physiology, Prentice Hall International Ltd 1st ed 1993, p. 600.)

2.3.2 Lung squeezing technique as a volume recruitment manoeuvre

This technique places emphasis on augmentation of airflow in the airways, and aims to assist mucus clearance from peripheral airways and improve regional ventilation. It composes of two phases:

2.3.2.1 Squeezing phase of lung squeezing technique

Squeezing phase is performed with three to four graded successive chest wall compressions which reduce the thoracic segment to near to full expiration position

The squeezing phase aims to increase the expiratory flow rate inside the small airways. These enhanced tidal breaths in the range of expiratory reserve volume are used to loosen and mobilize peripheral airway secretions. The manoeuvre emphasizes gentle compression and allows time for alveolar gas to escape through small airways by minimising excessive dynamic airway compression or closure which cause air-trapping.

Each squeezing manoeuvre incorporates a set of successive expiratory chest wall compressions forming three or four tidal breaths in the range of expiratory reserve volume, moving down to full expiration position (Figure 2.4). With the counteracting positive pressure delivered from the ventilator, a transient increase in the airway pressure may also help in maintaining the airway calibre, especially the small and narrowed airways.

During this squeezing phase, in order to generate adequate expiratory flow in the more proximal lobar bronchi, the gentle chest compression is delivered to a large thoracic region. The technique consists of placing the middle three fingers of one hand over the chest wall. Gentle pressure is delivered in an anteroposterior direction towards the trachea. Successive chest wall compressions are continued to give a total of three to four tidal breaths. The squeezing phase lasts for 4 to 6 seconds. As expiration progresses, the physiotherapist should feel that the chest wall is moving down the range of expiratory

reserve volume. Early resistance felt during this phase may indicate airtrapping as a result of compression of the collapsible segment of the airways, which is usually caused by excessive compression force or too fast compression. Gentle over-pressure is given at the end of the expiration which is followed immediately by the release phase.

2.3.2.2 Release phase of lung squeezing technique

Release phase is performed with a quick release of the compressed thoracic segment at the end of expiration

The release phase aims to recruit underventilated alveoli. This sudden release manoeuvre generates an sudden increase in transpulmonary pressure and facilitates opening of the alveoli. It also allows a quick rebound in the direction of the airflow inside the small airway, which may has a loosening effect on the mucus plugging the airway. Small airway closure may also be reduced with the opening up of the smallest bronchioles. The quick release phase intends to create a negative traction force on the small airways by utilising the recoil of the chest wall and lung parenchyma, and positive pressure delivered by the ventilator.

Following each release, a 2 to 3-second pause is allowed for the lung segments to expand to maximum without any external force before the application of another lung squeezing cycle (Figure 2.4).

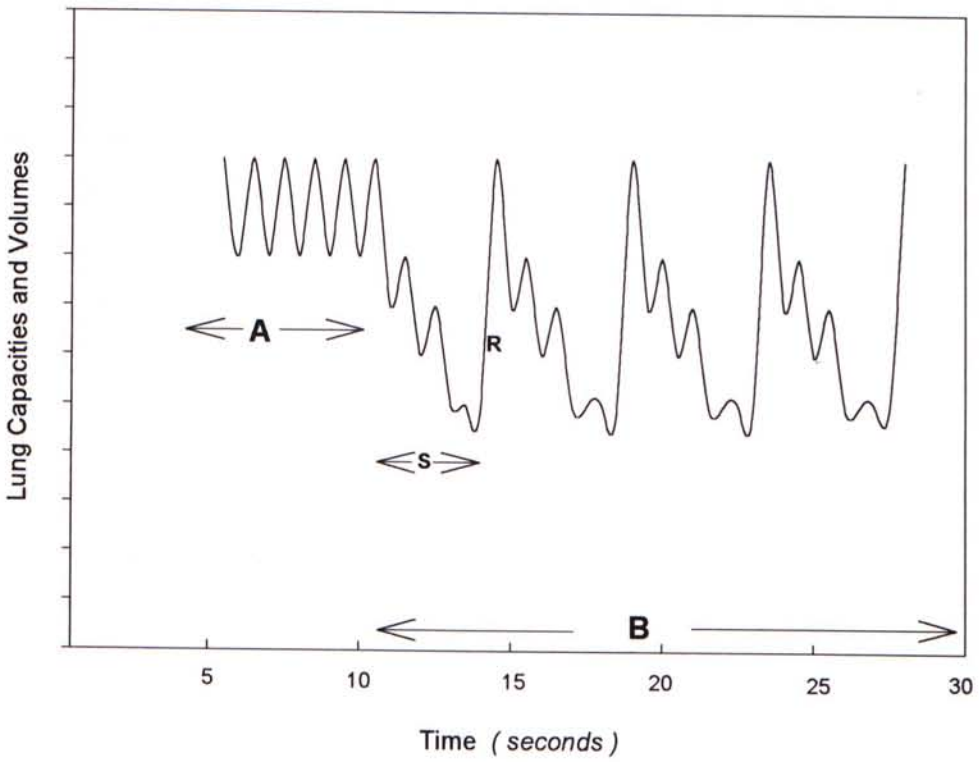


Figure 2-4: Diagrammatic representation of regional lung volume changes in ventilated infants during (A) Normal status (B) During chest physiotherapy with lung squeezing technique (LST)

3. Chapter 3 Physiotherapy Practice in Local Neonatal ICU

3.1 Current physiotherapy practice in Hong Kong Neonatal ICU settings

In a survey conducted by the Paediatric Special Interest Group, Hong Kong Physiotherapy Association (1996 unpublished data), a total of 102 physiotherapists replied to say that they had neonatal experience. All the respondents were requested to fill in a questionnaire in which all the questions had a four-point answer: frequent, occasional, rare and never options. 63 % of the respondents frequently treated neonatal chest conditions. With regard to the kind of treatment provided, the percentage of frequent users of percussion/vibration, suction, postural drainage (PD), and bagging were 86.3, 83.3, 79.4 and 66.7 respectively. The information revealed the current trend of physiotherapy in the Hong Kong neonatal settings. Chest condition was the most common indication for physiotherapy, and the traditional 'triad' modalities: percussion/vibration, PD and suction were the most commonly adopted physiotherapy methods.

3.1.1 Endotracheal suctioning protocol in Prince of Wales Hospital

There is a clinical protocol stating that suctioning should be performed in response to clinical signs and symptoms rather than a routine basis. Some of the criteria are:

- Desaturation
- Visualisation of secretion in endotracheal tube
- Requiring an increase in inflation pressure
- Increased irritability of the infant
- Bouts of coughing, "erratic" breathing, or fighting against the ventilator

Nurses will perform shallow suctioning for low-birth-weight infants ranging from one to four hours intervals. When blocking of the endotracheal tube is suspected, the nurses will perform suctioning prior to changing of the endotracheal tube is considered.

Hyperinflation, defined as the provision of an inspiratory volume up to 1.5 times tidal volume using a manual resuscitation bag (MRB), is not used routinely because of the risks of over-distension and iatrogenic air leaks. Bagging with a volume slightly in excess of the tidal volume, is reserved as a resuscitation means for irrecoverable bradycardia or severe oxygen desaturation.

Increased oxygenation with a FiO_2 greater than the prescribed level is frequently used before, during and after suctioning so as to maintain a SaO_2 level between 90 to 96%. The standard practice is to increase the FiO_2 level by 0.15 based on the response to suctioning. FiO_2 is then returned to previous level after the infant become stable.

Hyperventilation, defined as the provision of an increased number of breaths per minute, using a MRB or by increasing the ventilator rate, is not routinely used with suctioning. It is used only to counteract oxygen desaturation with or without accompanying bradycardia during or after suctioning.

3.1.1.1 Suctioning Procedures

Since several studies have reported the damaging effect of deep tracheal suctioning on the tracheal mucosal lining, shallow suctioning is performed by nurses as a routine practice. For physiotherapists, in order to be more effective in removing the secretion after physiotherapy manoeuvres, deep suctioning is still used. During suctioning, mechanical ventilation is suspended for 15 to 20 seconds. For size 2.5 and 3 endotracheal tube, a size 6 FG catheter (Pharmaplast) is inserted gently until meeting resistance. The catheter is then withdrawn slightly, followed by application of continuous suction pressure, and removal of the catheter in one continuous motion. The suctioning pressure ranges from 7 to 10 kpa negative pressure. If secretions are noted in the catheter, the procedure is repeated at least 30 seconds later, after all the vital signs have returned to the pre-suction condition.

0.9 % saline solution is instilled into the endotracheal tube before suctioning only if the secretions are tenacious. The volume used is 0.2 to 0.3 ml for preterm infants. Neither the neonatal nurses nor the physiotherapists routinely irrigate the endotracheal tube with saline solution before suctioning. Turning the head during suctioning for the purpose of reaching different sides of the bronchi, is not used.

Part II Main Study

4. Chapter 4 Research design

4.1 Ethics

The study was approved by the Ethical Committee for Clinical Research, the Chinese University of Hong Kong. The investigator understood that he had to take all the possible precautions so as to avoid any known potential injuries caused to the infants, was responsible to report any hazards that might occur during the course of the study.

4.2 Methods

4.2.1 Pilot study

Between January 1995 and May 1995, a pilot study was taken to refine the study design and evaluate the effects of the experimental treatment protocol. Totally seven neonates with mean (SD) gestational age 29.1 (3.2) weeks, presenting with lobar or whole lung atelectasis on a chest X-ray, were treated with the lung squeezing technique (LST). Two infants were ventilated with high frequency ventilator (HFV Infant Star ventilator), the other infants were on conventional mechanical ventilation (IPPV Infant Star ventilator). Six infants responded to LST with complete resolution of lung atelectasis. There were recurrence of lung collapse in three infants within one to three days, of which two infants had recurrence at the same site and one infant at a different area of the lung. All ten events of lung atelectasis responded to the experimental protocol with re-expansion of the atelectatic lobes which were evident on a chest X-ray after one to four treatment sessions (Table 4.1). One infant, presenting with left lung atelectasis five days post-patent ductus arteriosus ligation had ultrasound findings of left lung pleural effusion with associated atelectasis. This infant also developed gut perforation and was withdrawn from ventilatory support on fourteenth day post-operation because his condition was considered hopeless. There was no pulmonary complication noted in all cases. The result of the pilot study is summarised in Table 4.1

Table 4-1 *Result of pilot study on Lung Squeezing Technique (LST) protocol*

Subject	Gestational Age	Outcome	Area of Lung Collapse	Number of recurrence	Area of Lung Collapse (recurrence)	Treatment sessions required for First re-expansion	Treatment sessions required for complete resolution (including treatment for recurrence)
	week						
1	33	Survived	RUL	2	RUL	1	3
2[†]	24	Died	(L) Lung	0	-	-	-
3[†]	32	Survived	RUL	0	-	1	1
4	26	Survived	(R) Lung	1	(R) Lung	1	2
5	27	Survived	(L) Lung	0	-	1	1
6	32	Survived	(L) Lung	0	-	3	3
7	30	Survived	RUL	1	(L) Lung	4	5
Mean ± SD	29.1 ± 3.2						

[†] Infant on Infant Star HFV ventilator

4.2.2 Main study

4.2.2.1 Hypothesis

There is a difference in the efficacy of the lung squeezing technique and the conventional physiotherapy using a combination of postural drainage, percussion and vibration techniques in treating lung atelectasis in preterm infants on mechanical ventilation, as measured by the number of treatment sessions to attain first re-expansion of the atelectatic lung or lung lobe based on chest X-ray findings. A nondirectional hypothesis has been proposed.

4.2.2.2 Study Design

Study Patients

Between August 1995 and Jan 1998, all neonates with gestational age ≤ 37 weeks who required ventilatory support were enrolled if they satisfied the following criteria: (1) Presence of a segmental or lobar collapse confirmed on a CXR (2) Absence of major congenital malformation (3) Chest physiotherapy not contraindicated as determined by the attending neonatologist and (4) Granting of parental consent. All neonates enrolled into the study were checked for the level of the endotracheal tube on CXR by a neonatologist, so that the possibility of lung atelectasis being caused by inappropriate endotracheal tube insertion was excluded. The possibility of a thymus shadow being mistaken as upper lobe atelectasis on CXR was also ruled out.

Exclusion criteria

Infants with the following disease conditions were excluded from the study: persistent pulmonary hypertension of newborn, meconium aspiration syndrome, congenital heart

defects, pneumonia presenting with generalised patchy consolidation, post cardiothoracic surgery, hypoplastic lungs, pleural effusion and pneumothorax.

Infants with persistent pulmonary hypertension have very unstable pulmonary vascular response, even during the resolving stage. Maintenance of a satisfactory oxygen saturation is a main concern and physiotherapy procedures are contraindicated. The heterogeneous pattern of central and peripheral airway occlusion in meconium aspiration syndrome may render the outcome of physiotherapy techniques difficult to interpret. Congenital heart defects in infants result in a low and variable baseline oxygen saturation depending on the extent of right to left shunting and the complexity of the defects, which may make physiotherapy a hazardous procedure. The lung mechanics of hypoplastic lungs are very different from the normally developed lungs of preterm infants. Post cardiothoracic surgery cases were excluded since in these cases, the development of lung atelectasis and the effect of physiotherapy may be affected by structural malformation, oedema, or surgical trauma of the airways. Pneumonia cases were also excluded since the resolution of consolidation in these patients depends largely on the correction of the underlying infection by antibiotics. Infants with pleural effusion or pneumothorax were excluded since extrinsic pressure on the atelectatic lung might affect the treatment response.

Withdrawal criteria

Study subjects presented with marked haemodynamic instability due to other clinical reasons, requiring suspension of physiotherapy (as suggested by neonatologist in-charge) before the lung atelectasis resolved, were withdrawn from the study. Subjects who were complicated by pleural effusion, pneumothorax during the course of study before resolution of the lung atelectasis, or underwent any cardiothoracic surgery, were also withdrawn from the study.

Intra- and inter-examiner reliability

In this study, lung atelectasis and the site involved were confirmed by any one of the two specified neonatologists who were blinded to the study protocol. Both neonatologists had no knowledge about the grouping in this study. Follow-up chest radiographs were reviewed in the same manner.

Intra- and inter-examiner reliability on identification of lung atelectasis were assessed using 15 chest radiographs from three preterm infants with evidence of complete or resolved lung atelectasis. The two neonatologists designated to interpret the CXR for the study went through these radiographs, and completed a CXR review form (Appendix 1). The same process were repeated eight weeks later using the same set of CXR films, coefficient of agreement for neonatologist 1 and 2 were 0.93 and 0.87 respectively. Using Kappa statistic for chance agreement on a categorical scale (Portney and Watkins 1993a), intra-examiner reliability was calculated as $k = 83.33\%$ for neonatologist 1 and 59.38 for neonatologist 2. Inter-examiner reliability is 82.93%. These intra-examiner reliability values represented moderate level of agreement for neonatologist 2 and excellent agreement for neonatologist 1. The inter-examiner reliability represented excellent agreement between the two neonatologists.

Randomization and Sampling

Little is known about whether treatment response on high frequency ventilation is different from that of conventional ventilation. In order to investigate any interaction between the different modes of ventilation with the experimental protocol, randomization with stratification based on ventilation modes was used. Subjects were stratified into two queues based on the modes of ventilatory support as follows:

(1) Conventional ventilation, including Intermittent Positive Pressure Ventilation (IPPV) and Intermittent Mandatory Ventilation mode (IMV).

(2) High frequency ventilation, which includes high frequency ventilation (HFV) by flow interrupter, and high frequency oscillatory ventilation (HFOV) generated by a moving piston.

Conventional ventilation were delivered by Infant Star neonatal ventilator (Infrasonics, Inc., San Diego, CA), a time cycled, pressure limited ventilator. HFV was delivered by HFV Infant Star ventilator (Infrasonics, Inc.). HFOV was delivered by Sensormedics oscillatory ventilator model 3100A.

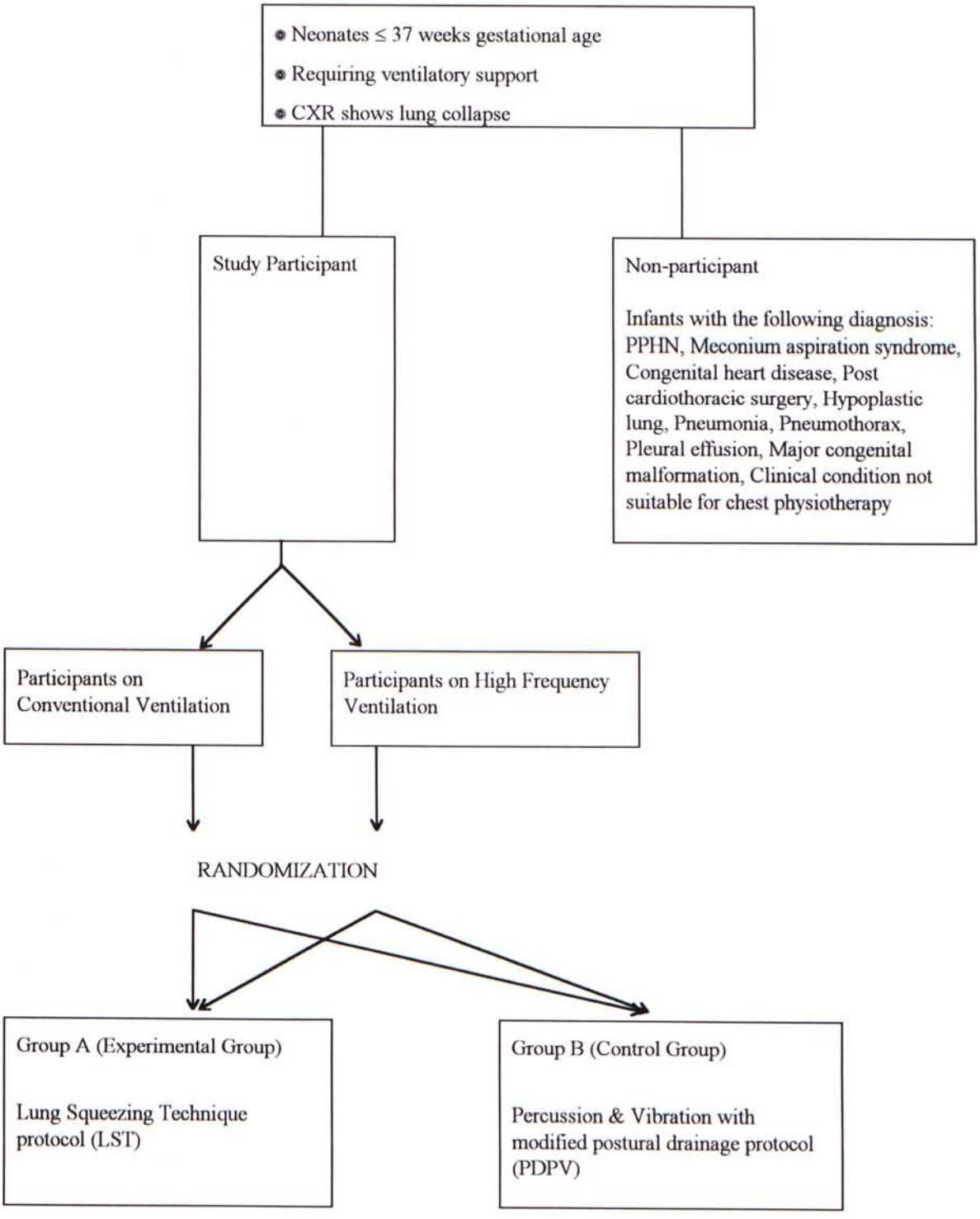
Sample size is determined to be 26 in each group (Portney and Watkins 1993b), based on a type I error $\alpha_2 = 0.05$ and type II error $\beta = 0.20$ (power = 0.8). Since the hypothesis does not predict which treatment protocols will be superior, a nondirectional alternative hypothesis is used. A large effect size d = 0.8 is used, which represents a great degree of separation. This means that we need a difference between the two sample means with more than 80% of the standard deviation before we consider there is a clinically meaningful difference between the two groups . Sample allocation into two groups is based on queue derived from a table of random numbers and allocate into two groups:

Group A: Experimental group using lung squeezing technique protocol (LST)

Group B: Control group using the conventional postural drainage, percussion and chest vibration protocol (PDPV)

The study design is summarised in the following flowchart (Figure 4.1).

Figure 4-1: Study Design for the evaluation of chest physiotherapy techniques in correcting lung atelectasis in preterm infants on mechanical ventilation



4.3 Methodology

4.3.1 Treatment protocol

4.3.1.1 Experimental Group protocol

Lung squeezing technique was defined as three to four graded successive chest wall compressions to a particular thoracic region followed by a quick release of the compression force. The technique was performed to three regions bilaterally namely, upper zone, anterior lower and posterior lower zone in supine position, with no body tilt, for 10 minutes.

The details of practical application of the technique was discussed in section 2.3.2

4.3.1.2 Control Group protocol

Percussion and vibration in modified postural drainage positions were performed with the infant lying alternately on the two sides, with no body tilt, for 10 minutes.

Physiotherapy procedures were performed by the investigator (INC Wong) whenever possible. Treatment sessions were delivered twice daily, one in the morning and one in the afternoon. On the day of enrolment, however, only one treatment was given to infants who were enrolled in the afternoon. If for any reason when the investigator was not available, another physiotherapist who had completed a neonatal in-service training program was assigned to treat the subject according to the stated protocol. The substituted physiotherapists however had no knowledge of the study otherwise.

The nurses, and physiotherapists other than the investigator (INC Wong) had no knowledge about the study.

4.3.2 Outcome Measure

4.3.2.1 Chest X-ray

In this study, all chest radiographs were in the format of paired phosphor images. The result of chest X-ray were analysed by either of the two designated neonatologists. The first chest X-ray after first treatment session was taken between two to three hours to evaluate the initial response of the lung atelectasis. Subsequently, CXR was performed whenever clinically indicated, usually when the infant showed signs of deterioration of the respiratory status such as: significant increase in FiO_2 or ventilator settings, significant increase in frequency or severity of bradycardia and desaturation. A post-treatment chest X-ray was taken routinely 3 days after lung re-expansion occurred, so as to detect any recurrence. Number of treatment sessions to attain first re-expansion of the collapsed area was noted. If there was a recurrence of atelectasis within 3 days, either on the same site or a different site, the total number of treatment sessions would count all the sessions starting from the first session till complete resolution of any atelectasis (Figure 4.2).

4.3.2.2 Other Measurements

Ventilator parameters including FiO_2 and peak inspiratory pressure were noted at 6 hours post first treatment sessions.

Pre and post treatment arterial blood gas (ABG) were taken within 3 hours before and after each treatment by other medical staff.

Physiological parameters during the first treatment session were used to evaluate the physiological response of the infant to the two different protocols. Heart rate, systolic blood pressure, diastolic blood pressure, mean blood pressure and oxygen saturation reading during treatment were recorded by the investigator. Since there were continuous fluctuations of the reading throughout a treatment session, only the values with the greatest deviation from the pre-treatment baseline were recorded. Data collection for quantitative comparison was restricted to the time gaps in between active lung squeezing

or percussion and vibration, and did not include any changes during endotracheal suctioning. Adverse events such as hypotension (mean blood pressure < 30 mmHg), desaturation (< 80%) or bradycardia requiring hand ventilation were also recorded. Other pulmonary complications observed during the course of study were also recorded, which included any pulmonary haemorrhage, pneumothorax and other air leak syndromes.

Also recorded were the duration of mechanical ventilation, duration of oxygen dependency, diagnosis of bronchopulmonary dysplasia defined as oxygen dependency at 36 weeks post-conception, presence of intra-ventricular haemorrhage detected by routine cranial ultrasound, and mortality. These data were documented on a specially designed data sheet (Appendix II).

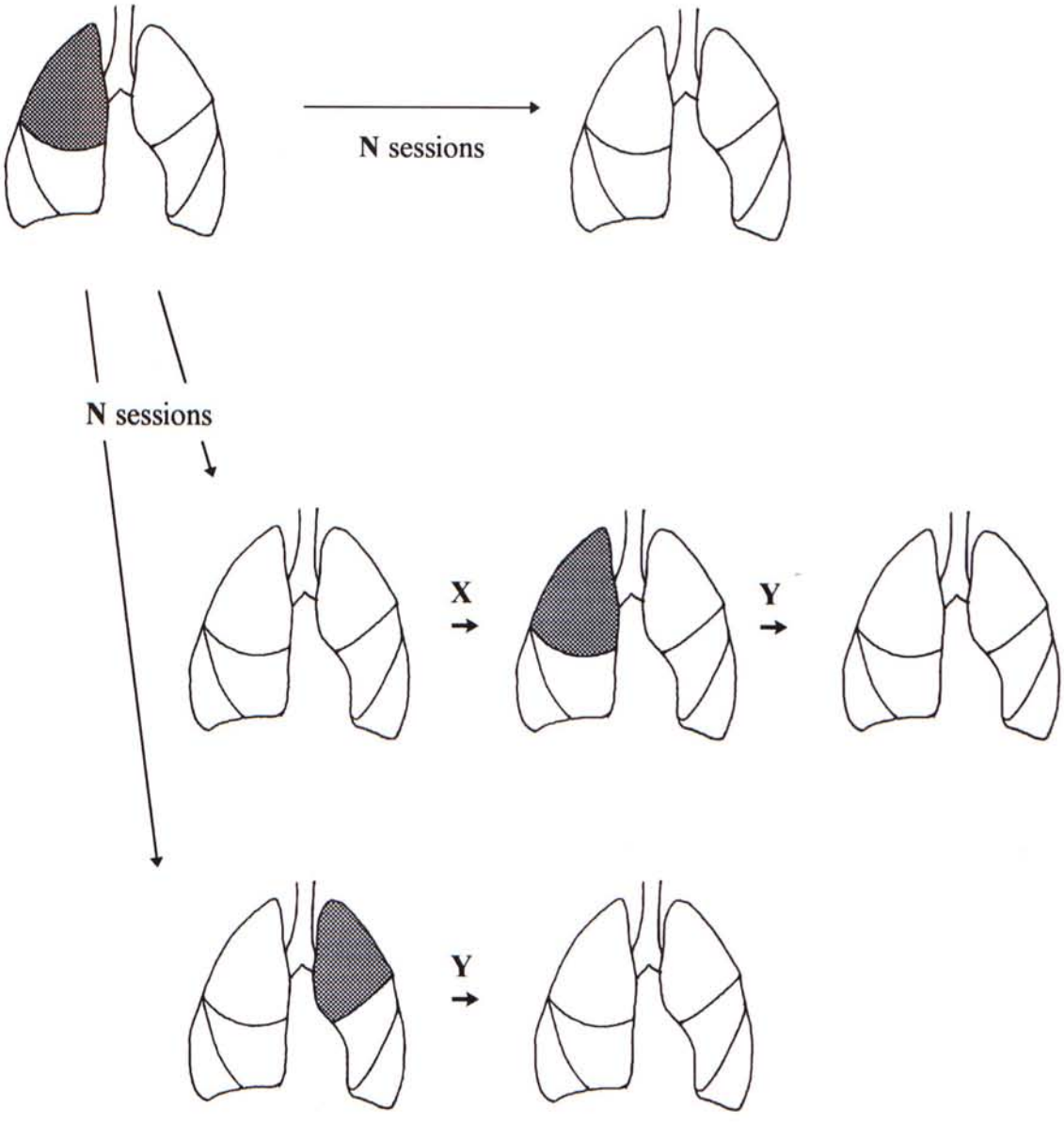


Figure 4-2: Diagram showing the method of calculation of the number of treatment session required to attain first re-expansion (S_1) and total resolution (S_T) of lung atelectasis.

First row: Re-expansion without recurrence of lung atelectasis, both S_1 and S_T equal to N. Second row: recurrence of lung atelectasis after first re-expansion, S_1 equal to N, S_T equal to (N+X+Y). Third row: recurrence of lung atelectasis at a different site whereas the original site was re-expanded, S_1 equal to N, S_T equal to (N+Y).

4.3.3 Statistics

Distribution of lung atelectasis in the two treatment groups are compared by χ^2 test. The number of treatment sessions required to attain first re-expansion and total resolution of lung atelectasis are compared between groups by Mann-Whitney Rank Sum test. Groups with infants that died with unresolved collapsed lung are analysed twice, one with the unresolved cases excluded, one with the unresolved cases converted to a number with greatest rank in all Mann-Whitney Rank Sum test.

Distribution of recurrence of lung collapse between the two groups is analysed by χ^2 test. Infants that died with collapsed lung are excluded during analysis. Further analysis of characteristics of recurrence are performed by χ^2 test.

Factors correlated with resolution of atelectasis are analysed by Spearman Rank Sum Correlation test. These include selected demographic characteristics, duration of mechanical ventilation and oxygen dependency.

Ventilator parameters before first treatment session, including FiO_2 and peak inspiratory pressures, are compared between treatment groups with unpaired *t*-test or Mann-Whitney Rank Sum test. Pre and post treatment values are analysed with paired *t*-test or Wilcoxon Signed Rank test. Differences from their baseline after first treatment are compared between treatment groups, using Mann-Whitney Rank Sum test.

For arterial blood gas values, heart rate, blood pressure parameters and SaO_2, pre and post treatment values are compared using paired *t*-test or Wilcoxon Signed Rank test within group. Differences from their baseline after treatment are compared between groups, using Mann-Whitney Rank Sum test.

The number of adverse events including hypotension, desaturation requiring hand ventilation are analysed by χ^2 test or Fisher Exact test.

Unpaired *t*-test or Mann-Whitney Rank Sum test are used to analyse duration of mechanical ventilation and oxygen dependency. Other clinical outcome including occurrence of intra-ventricular haemorrhage, bronchopulmonary dysplasia and mortality are analysed by χ^2 test or Fisher Exact test. Progression of intra-ventricular haemorrhage are analysed by McNemar's test.

All χ^2 test are adjusted with Yates' correction for continuity. When the expected observations of one or more cells in the contingency tables are less than five, Fisher's exact test is used instead of χ^2 test. All continuous data are analysed by normality test prior to comparison. When normality test fails, unpaired *t*-test is substituted by Mann-Whitney Rank Sum test whereas paired *t*-test is substituted by Wilcoxon Signed Rank test. All parametric data are expressed as mean $\pm$ SD. Non-parametric data are expressed as median, (25^{th}, 75^{th} percentiles). For all the data, differences are considered significant for rejection of the null hypothesis at $p < 0.05$. All analysis are carried out using statistical computer program (Sigmastat, Jandel Scientific, San Rafael, CA) and graphics are derived by a scientific graphing software (Sigmaplot, Janel Scientific).

5. Chapter 5 Results

5.2 Demographic Data

A total of 56 preterm infants were enrolled in the study. They had a mean (SD) gestational age 28.1 (3.3) weeks (range 22.7 to 36.6 weeks), and birth weight ranging from 540 g to 2,900 g (1039 ± 466 g, mean ± SD). Their demographic characteristics were summarised in Table 5.1. There were no significant difference between the two groups in their gestation, birth weight, body weight at study, or ventilation parameters.

Gestational age of infants are presented by Tukey box plot Figure 5.1. Body weight of infants at birth and at time of the study are presented by Figure 5.2. Demographic characteristics of the infants based on stratification by mode of ventilation are presented by Figure 5.3.

Two infants were withdrawn from the study, one from the experimental group and one from the control group. The one in the experimental group presented with left lung collapse, received one session of lung squeezing, but bronchial toilet was performed within half an hour before the first chest X-ray was taken. This infant underwent a patent ductus arteriosus ligation procedure on the next day. The one in the control group presented with a right upper lobe collapse, received two sessions of percussion, vibration and postural drainage protocol. Post treatment chest X-ray showed marked hazziness of bilateral lung fields especially on left side. His general condition deteriorated within the same day and required FiO_2 of 1.00 and nitric oxide therapy. Physiotherapy was suspended in view of his critical condition.

Table 5-1 *Demographic features of infants and ventilator parameters Comparison between LST and PDPV group*

	LST Group n = 26	PDPV Group n = 30	p Value
Demographic characteristics			
Gestational age (weeks)	27.9 ± 2.9	28.3 ± 3.7	0.656*
min	23.9	22.7	
max	36.6	35.9	
B.W. at birth (g)	1042 ± 472	1036 ± 469	0.706*
min	585	540	
max	2900	2046	
B.W. at recruit (g)	1265 ± 544	1157 ± 557	0.332†
min	650	540	
max	2970	2700	
Number of lobes with lung atelectasis	29	32	
Ventilator parameters			
FiO_2	0.40 (0.25, 0.50)	0.40 (0.28, 0.60)	0.755†
Peak Inspiratory Pressure (cm H_2O)	14 (9, 19)	15 (11, 19)	0.828*
Number on IPPV	11	16	
Number on HFV	9	7	
Number on HFOV	6	7	

* unpaired t-test
† Normality test failed, Mann-Whitney Rank sum test is used
Values are expressed as mean±SD or median (25^{th}, 75^{th} percentiles)

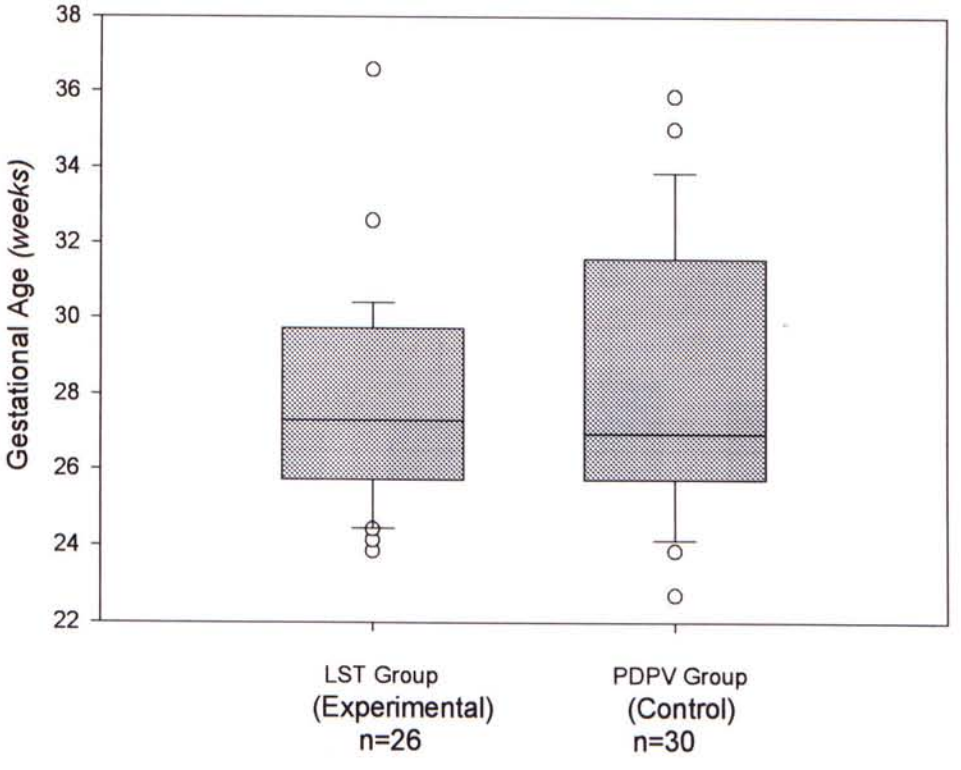


Figure 5-1: Gestational age. Comparison between LST and PDPV group
Box plots indicate the 25th, 50th, and 75th percentile of the illustrated data.

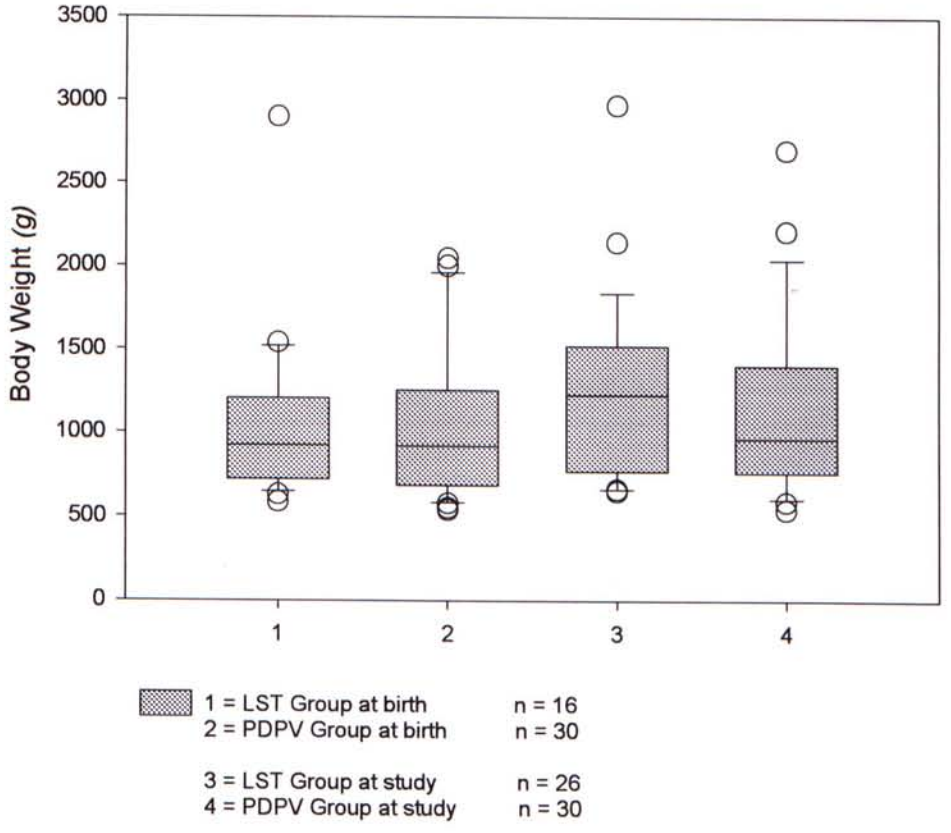


Figure 5-2: Body weight. Comparison between LST and PDPV group at birth and at the time of study

Box plots indicate the 25th, 50th, and 75th percentile of the illustrated data.

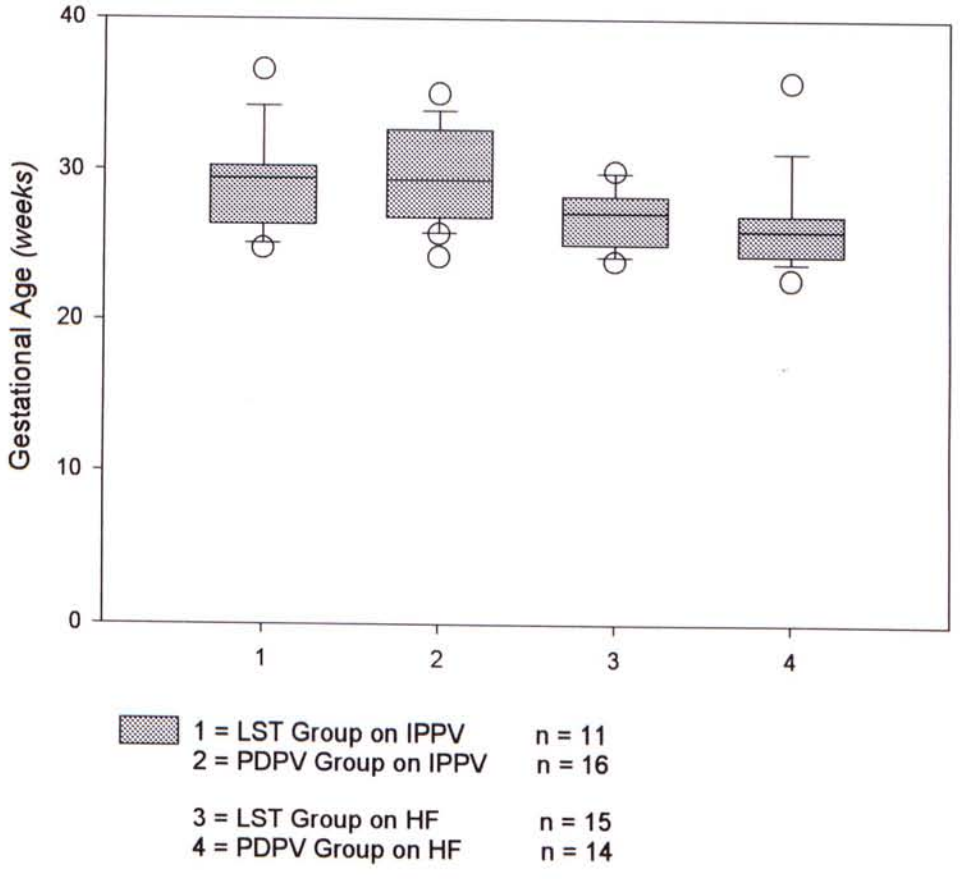


Figure 5-3: Gestational age. Comparison between LST and PDPV group based on stratification by mode of ventilation.

IPPV = conventional ventilation. HF = high frequency ventilation. Box plots indicate the 25th, 50th, and 75th percentile of the illustrated data.

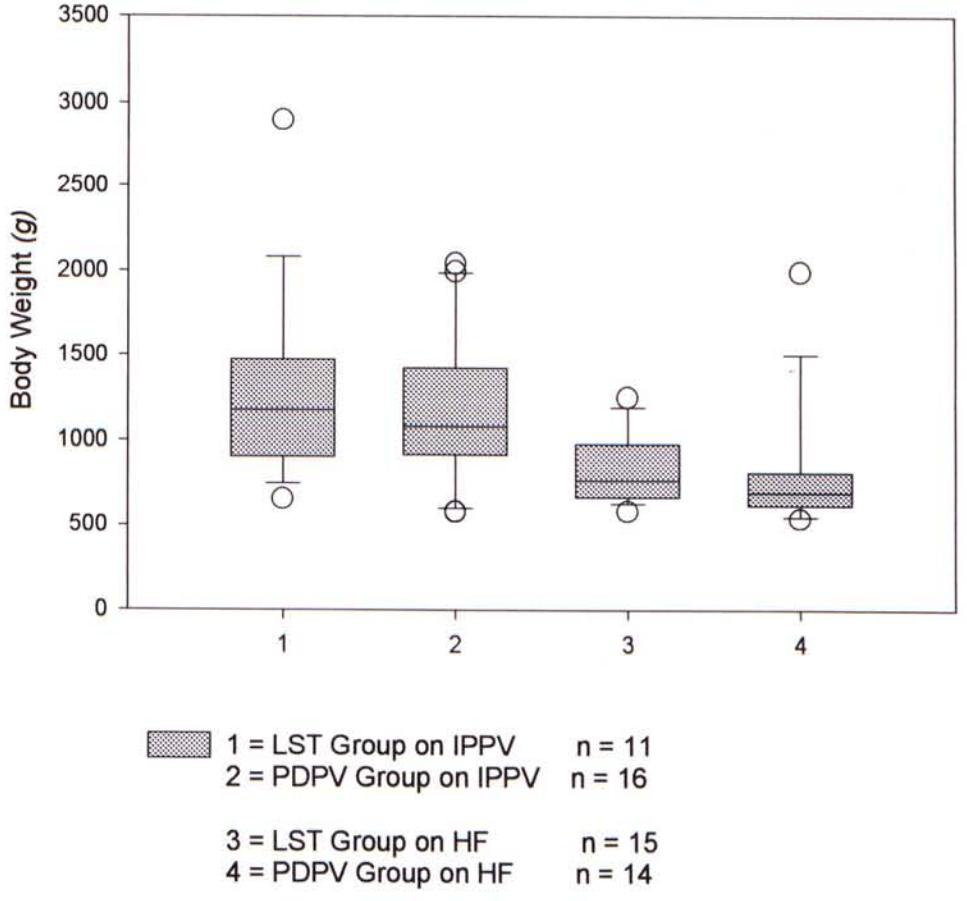


Figure 5-4: Body weight. Comparison between LST and PDPV group based on stratification by mode of ventilation

IPPV = conventional ventilation. HF = high frequency ventilation. Box plots indicate the 25th, 50th, and 75th percentile of the illustrated data.

5.3 Resolution of lung atelectasis

5.3.1 Distribution of lung atelectasis

Distribution of lung atelectasis was summarised in Table 5.2 and Figure 5.5. Right upper lobe (RUL) with or without other area of involvement was the commonest site of lobar collapse, accounting for 66% and 75% of the total number in the LST group and PDPV group respectively. There were 6 infants in the LST group and 5 infants in the PDPV group who had more than one atelectatic lobe before intervention. The distribution pattern of atelectasis among the various lung lobes was not significantly different between the two groups (Chi-square = 1.972, df 5, $p = 0.853$)

Table 5-2 *Summary of distribution of lung atelectasis among the lung lobes*

Site of lung atelectasis	LST Group n=26	PDPV Group n=30
Right Upper lobe	19 (66)	24 (75)
Right Middle lobe	3 (10)	2 (6)
Right Lower Lobe	1 (3)	1 (3)
Right Lung	2 (7)	2 (6)
Left Upper Lobe	1 (3)	2 (6)
Lingula	0 (0)	0 (0)
Left Lower Lobe	0 (0)	0 (0)
Left Lung	3 (10)	1 (3)
Subjects with one lobe involved	n=20	n=25
Subjects with more than one lobe involved	n=6	n=5

Numbers are expressed as count (%)
Chi-square test is used to compare site of atelectasis. Chi-square = 1.972, df 5, $p = 0.853$

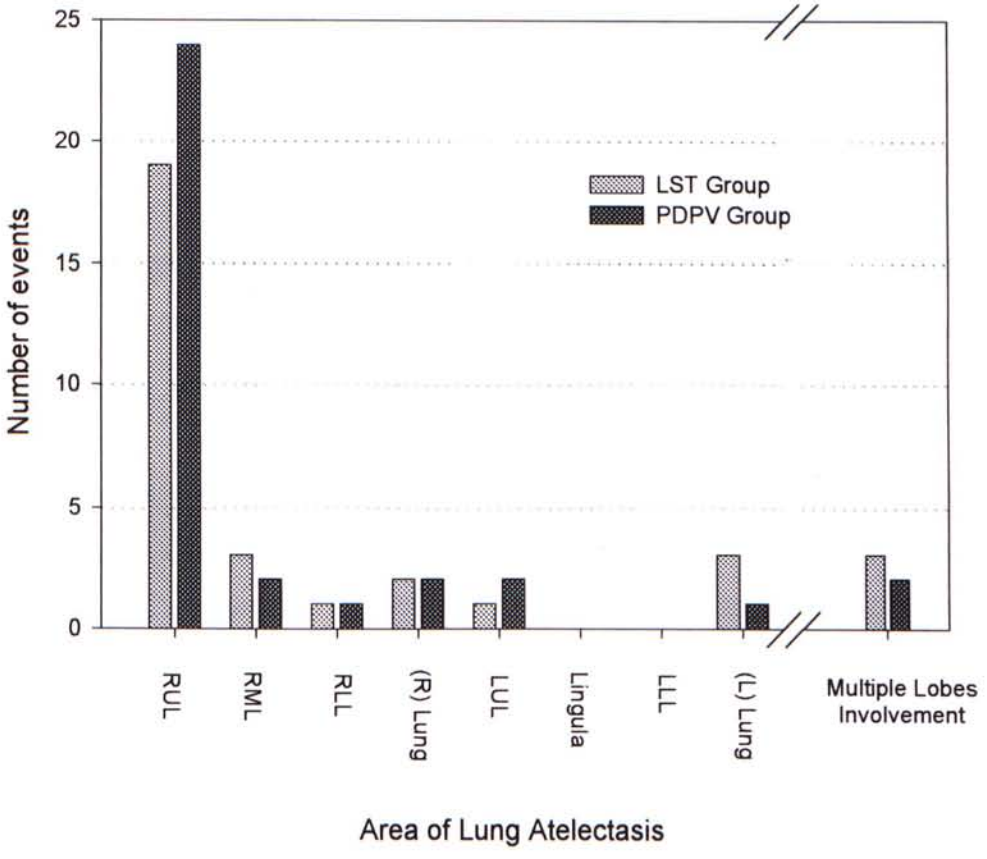


Figure 5-5: Distribution of lung atelectasis. Comparison between LST and PDPV group.

RUL = right upper lobe RML = right middle lobe RLL = right lower lobe LUL = left upper lobe LLL = left lower lobe

5.3.2 First re-expansion of lung atelectasis

The number of physiotherapy sessions to attain *the first re-expansion of the atelectatic site* were given in Figure 5.6 and Table 5.3.

Resolution of atelectasis was achieved in 21 infants in the LST group, and 7 infants in the PDPV group after 1 session of treatment. The lung atelectasis in 4 infants in the PDPV group failed to resolve after treatment was continued for 3, 4, 4, and 7 treatment sessions respectively, before they died of critical clinical conditions. Comparison was made using Mann Whitney Rank Sum test after converting these unresolved cases to the highest rank. The number of treatment session required to attain first re-expansion of the atelectatic lung/lobes was significantly smaller in the LST group when compared between the groups as a whole ($p < 0.001$) or between infants receiving the same type of assisted ventilation in the two groups ($p < 0.05$).

In order to evaluate whether different modes of ventilation had any effect on the efficacy of the techniques, comparison between infants receiving HF and IPPV within the same group (Table 5.4) was made. The results showed that the mode of ventilation did not affect the number of treatment session required to achieve the first re-expansion.

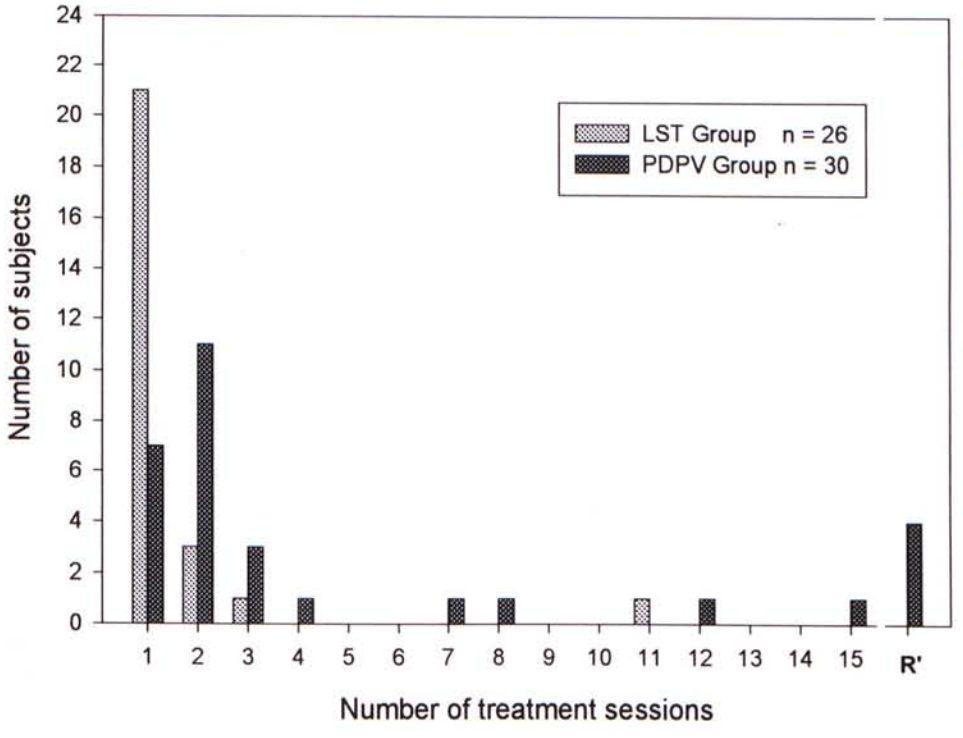


Figure 5-6: Treatment sessions to attain first re-expansion of lung atelectasis. Comparison between LST and PDPV group.
R' = Unresolved atelectasis

Table 5-3 *Number of treatment sessions to attain first re-expansion of lung atelectasis Comparison between LST and PDPV Group*

Number of treatment session to attain 1st re-expansion	LST Group		PDPV Group		*p* value
All infants	1 (1, 1)	n=26	2 (1, 3)	n=30*	<0.001†
IPPV	1 (1, 1)	n=11	2 (1, 2)	n=16*	0.006†
HF	1 (1, 1.8)	n=15	2 (2, 4)	n=14	0.006

Normality test failed, Mann-Whitney Rank Sum test is used
Values are expressed as median (25^{th}, 75^{th} percentiles)
* Including 4 unresolved cases
† p values after converting unresolved cases to largest rank number

Table 5-4 *Number of treatment sessions to attain first re-expansion of lung atelectasis Comparison of different ventilation mode within group*

		Conventional (IPPV)		High frequency (HF)		*p* value
Number of treatment sessions to attain 1st re-expansion	LST Group	1 (1, 1)	n=11	1 (1, 1.8)	n=15	0.432
	PDPV Group	2 (1, 2)	n=16*	2 (1, 2)	n=14	0.851†

Normality test failed, Mann-Whitney Rank Sum test is used
Values are expressed as median (25^{th}, 75^{th} percentiles)
* Including 4 unresolved cases
† p values after converting unresolved cases to largest rank number

5.3.3 Complete resolution of lung atelectasis

The results obtained from subsequent chest X-rays were analysed. Complete resolution of lung atelectasis was defined as *clearing of the lung fields without recurrence of atelectasis within three days of treatment* . The calculation of number of sessions is explained in details in page 46. Recurrence of lung atelectasis occurred at more than three days after complete resolution was not counted. The results are summarised in Figure 5.7 and Table 5.5.

There were 2 unresolved cases in the LST group, both receiving HF ventilation, and 4 unresolved cases in the PDPV group, all being ventilated by the IPPV group. The number of sessions required to attain complete resolution of lung atelectasis were not significantly different between the two groups ($p = 0.059$). The difference however became significant when only infants receiving IPPV in the two groups were compared ($p = 0.012$).

Comparison of infants receiving HF and IPPV within same group also showed that in the LST group infants receiving IPPV required significantly fewer sessions than those receiving HF ($p = 0.031$). There was no significant difference in the efficacy of PDPV between infants receiving the two types of ventilation (Table 5.6).

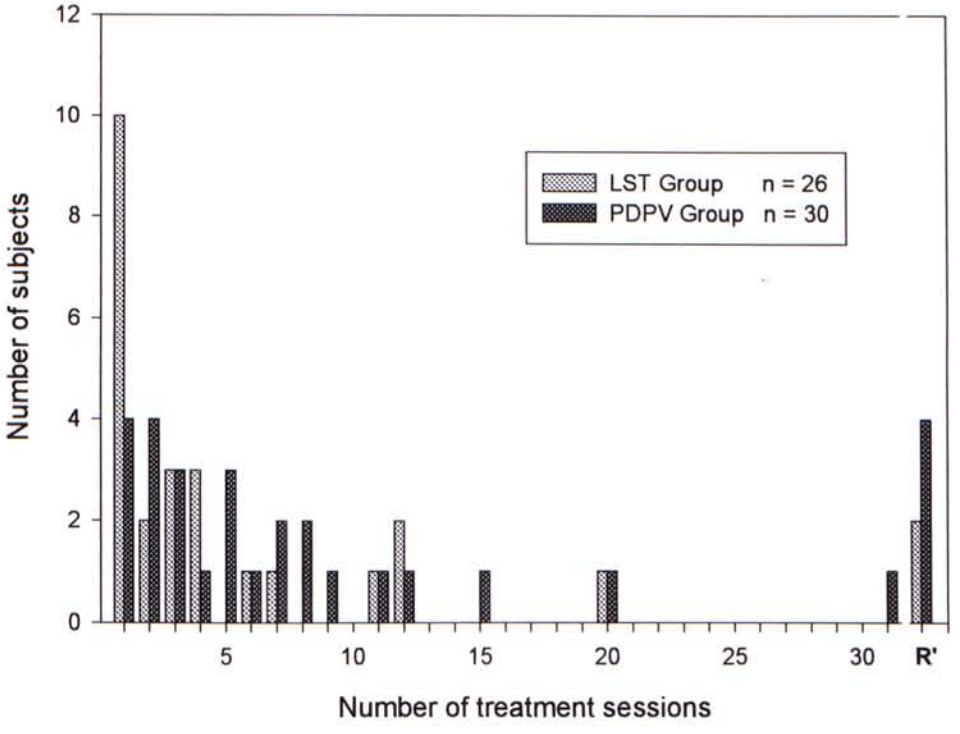


Figure 5-7: Treatment sessions to attain complete resolution of lung atelectasis Comparison between LST and PDPV group.
R' = Unresolved cases

Table 5-5 *Number of treatment sessions to attain complete resolution of lung atelectasis*

Comparison between LST and PDPV group

Number of treatment session to attain complete resolution of atelectasis	LST Group		PDPV Group		*p* value
All infants	2.5 (1, 5)	n=26[+]	5 (2, 8)	n=30*	0.059[†]
IPPV	1 (1, 3)	n=11	3 (2, 6)	n=16*	0.012[†]
HF	4 (1, 11.5)	n=15[+]	6.5 (3, 11)	n=14	0.948[†]

Normality test failed, Mann-Whitney Rank Sum test is used
Values are expressed as median (25^{th}, 75^{th} percentiles)
+ Including 2 unresolved cases
* Including 4 unresolved cases
† p values after converting unresolved cases to largest rank number

Table 5-6 *Number of treatment sessions to attain complete resolution of lung atelectasis*

Comparison of different ventilation mode within group

		Conventional (IPPV)		High frequency (HF)		*p* value
Number of treatment sessions to attain complete resolution of lung atelectasis	LST Group	1 (1, 3)	n=11	4 (1, 11.5)	n=15[+]	0.031[†]
	PDPV Group	3 (2, 6)	n=16*	6.5 (3, 11)	n=14	1.000[†]

Normality test failed, Mann-Whitney Rank Sum test is used
Values are expressed as median (25^{th}, 75^{th} percentiles)
* Including 4 unresolved cases
† p values after converting unresolved cases to largest rank number

5.3.3.1 Sites of recurrence of lung atelectasis

The site of recurrence of lung atelectasis in the two treatment groups were presented as a scatter graph Figure 5.8. Statistical comparison between the two groups did not show any significant difference in the site or pattern of recurrence (Table 5.7).

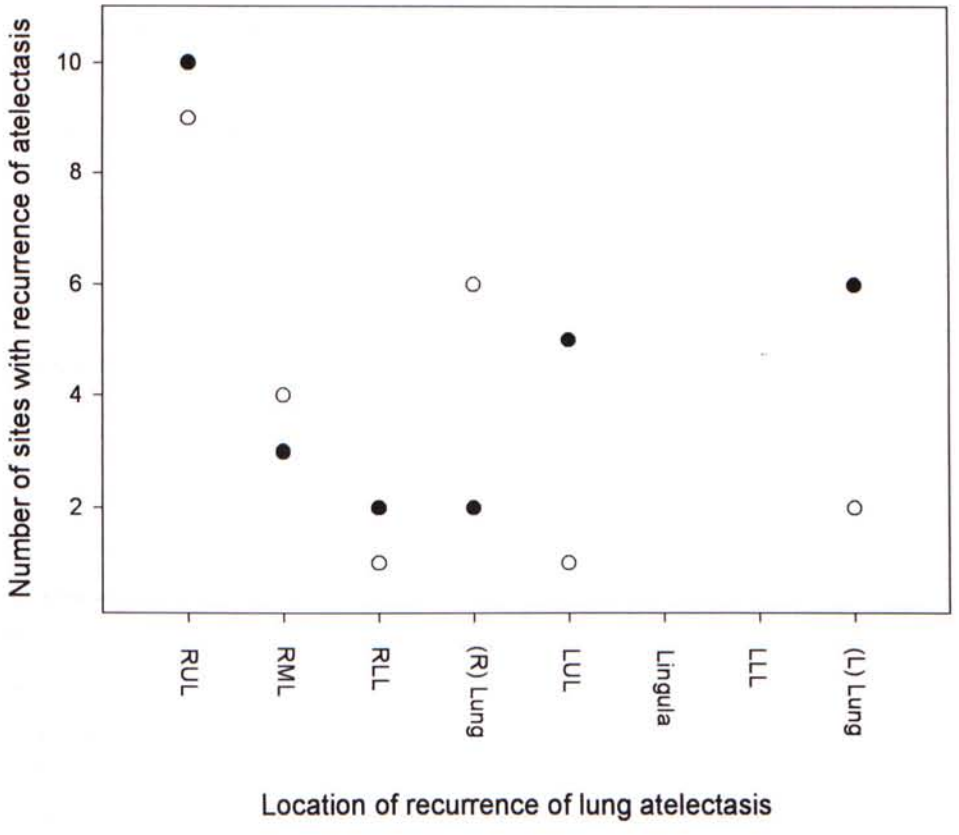


Figure 5-8: Distribution of site of recurrence of lung atelectasis.
RUL = right upper lobe RML = right middle lobe RLL = right lower lobe LUL = left upper lobe LLL = left lower lobe

Table 5-7 *Distribution of recurrence of lung atelectasis*

		LST Group	PDPV Group	Chi-Square value	df	*p*-value
		n=26	n=30			
Infants with recurrent atelectasis	Yes	14 (28)	14[+] (23)	0.774	1	0.781
	No	12	12			
Infants with recurrence at same site	Yes	9 (10)	8 (8)			1.000
	No	5	6			
Infants with recurrence at different site	Yes	10 (18)	11 (15)			1.000
	No	4	3			
Infants with additional atelectatic lobe involved	Yes	6	6	0.146	1	0.703
	No	8	8			

Values are expressed as number of subjects (number of sites of lung atelectasis)
+ excluding 4 unresolved cases

5.4 Factors correlated with number of treatment sessions required to attain resolution of atelectasis

The number of treatment sessions to attain first re-expansion (S_1) and total resolution (S_T) of lung atelectasis were examined to determine its association with some of the demographic characteristics of the infants which affect the size and development of the small airways. These factors included gestational age, body weight at birth and at recruitment, and postnatal age. The association between the required number of treatment sessions and the duration of mechanical ventilation and oxygen dependency were also examined to assess whether these known risk factors for chronic lung disease might affect the efficacy of the treatment protocol.

The findings showed that in the LST group, the number of required treatment sessions to attain first re-expansion of atelectasis (S_1) was inversely related to birth weight at birth ($p = 0.048$). The correlation with gestation showed a similar tendency although statistically insignificant ($p = 0.078$). No significant correlation with other variables examined was noted (Table 5.8). In the PDPV group, there is no significant relationships between S_1 with any of the variables (Table 5.9).

In the LST group, the number of treatment sessions required to attain complete resolution (S_T) appeared to be inversely related to gestation, body weight at birth and at recruit, but their correlation did not reach statistical significance (p-values 0.068, 0.082 and 0.073 respectively) (Table 5.10). In the PDPV group, there was a positive correlation between S_T .and the duration of mechanical ventilation ($p = 0.039$) and duration of oxygen dependency ($p = 0.006$). (Table 5.11, Figure 5.9 and 5.10)

Table 5-8 *Correlation between number of treatment sessions to attain first re-expansion of atelectasis to gestation, birth weight, body weight and postnatal age at recruit, duration of mechanical ventilation, and oxygen dependency in LST Group*

Variable			Correlation coefficient	*p* value
1	Gestation	n=26	-0.35	0.078
2	Body weight at birth	n=26	-0.39	0.048 *
3	Body weight at recruit	n=26	-0.26	0.193
4	Age at recruit	n=26	0.17	0.391
5	Duration of mechanical ventilation	n=21	0.25	0.279
6	Duration of oxygen dependency	n=19	0.03	0.900

Table 5-9 *Correlation between number of treatment sessions to attain first re-expansion of atelectasis to gestation, birth weight, body weight and postnatal age at recruit, duration of mechanical ventilation, and oxygen dependency in PDPV Group*

Variable			Correlation coefficient	*p* value
1	Gestation	n=26	-0.25	0.225
2	Body weight at birth	n=26	-0.24	0.245
3	Body weight at recruit	n=26	-0.28	0.165
4	Age at recruit	n=26	0.15	0.466
5	Duration of mechanical ventilation	n=20	0.13	0.577
6	Duration of oxygen dependency	n=19	0.30	0.216

* $p < 0.05$ † $p < 0.01$

Table 5-10 *Correlation between number of treatment sessions to attain complete resolution of atelectasis to gestation, birth weight, body weight and postnatal age at recruit, duration of mechanical ventilation, and oxygen dependency in LST Group*

Variable		Correlation coefficient	*p* value
1 Gestation	n=24	-0.38	0.068
2 Body weight at birth	n=24	-0.36	0.082
3 Body weight at recruit	n=24	-0.371	0.073
4 Age at recruit	n=24	-0.10	0.650
5 Duration of mechanical ventilation	n=20	0.34	0.145
6 Duration of oxygen dependency	n=18	0.10	0.699

Table 5-11 *Correlation between number of treatment sessions to attain complete resolution of atelectasis to gestation, birth weight, body weight and postnatal age at recruit, duration of mechanical ventilation, and oxygen dependency in PDPV group*

Variable		Correlation coefficient	*p* value
1 Gestation	n=26	-0.10	0.625
2 Body weight at birth	n=26	-0.12	0.553
3 Body weight at recruit	n=26	-0.18	0.369
4 Age at recruit	n=26	0.29	0.156
5 Duration of mechanical ventilation	n=20	0.47	0.039*
6 Duration of oxygen dependency	n=19	0.60	0.006†

* $p < 0.05$ † $p < 0.01$

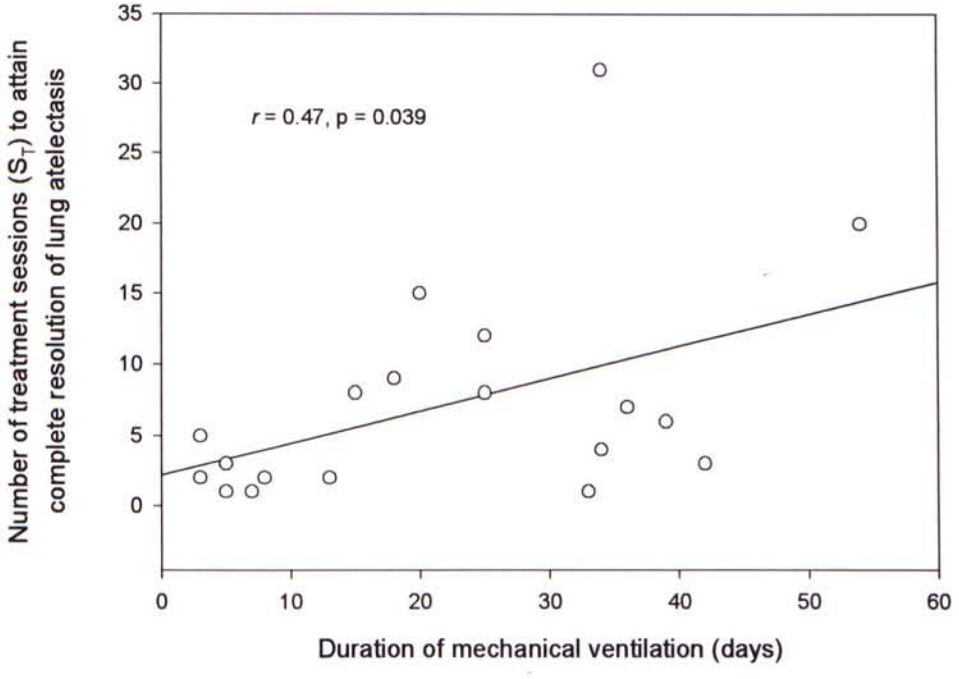


Figure 5-9: Number of treatment sessions (S_T) to attain complete resolution of lung atelectasis in relation to duration of mechanical ventilation in PDPV group.

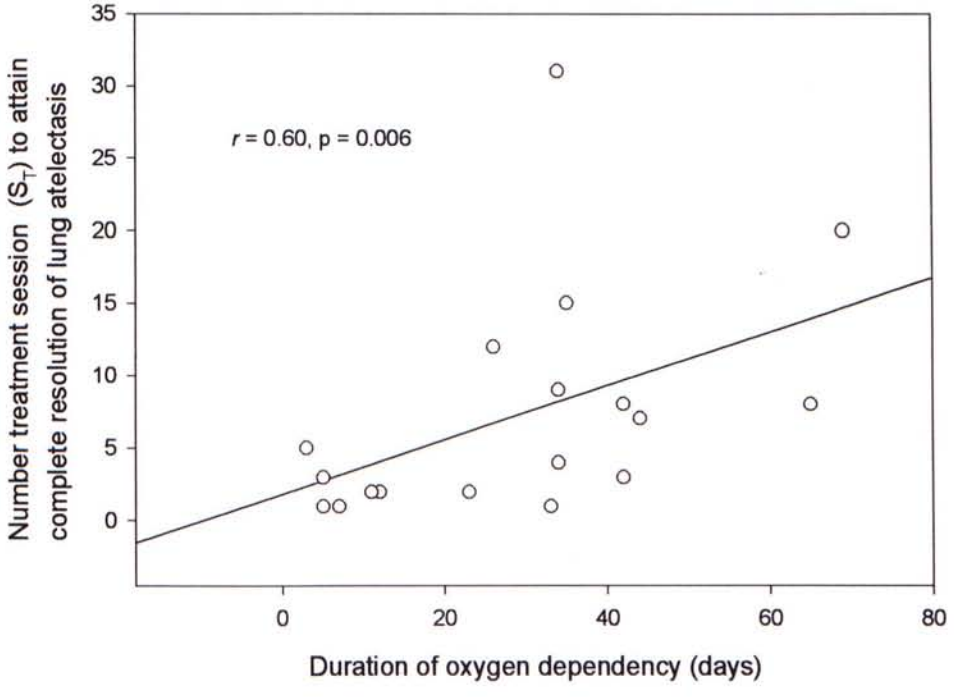


Figure 5-10: Number of treatment sessions (S_T) to attain complete resolution of lung atelectasis in relation to duration of oxygen dependency in PDPV group.

5.5 Ventilator parameters changes

The two groups had similar ventilator parameters including FiO_2 and peak inspiratory pressure before the first treatment (Table 5.12).

Treatment effect was analysed by comparing differences of values at first intervention and at 6 hours post first treatment session. Changes in ventilator parameters at 6 hours post first treatment session between the two groups were also compared (Table 5.13). There were decrease in FiO_2 and peak inspiratory pressure in both groups, although the difference was not statistically significant. There was no significant difference in changes in ventilator parameters between the two groups.

Table 5-12 *Ventilator parameters at first treatment: Comparison between LST and PDPV Group*

	LST Group n = 26	PDPV Group n = 30	*p* value
FiO_2	0.40 (0.25, 0.5)+	0.40 (0.28, 0.6)+	0.755+
Peak Inspiratory Pressure *cm H_2O*	14.8 ± 5.8*	15.2 ± 5.7*	0.828*

+ Normality test failed, Mann-Whitney Rank Sum test is used
Values are expressed as median (25^{th}, 75^{th} percentiles)
* Normality test passed P=0.133, Equal variance test P=0.262, t-test is used
Values are expressed as mean ± SD

Table 5-13 *Changes in ventilator parameters at 6 hours post first treatment session Comparison between LST and PDPV Group*

		pre	post	*p* value
LST Group n = 26	FiO_2	0.4 (0.25, 0.5)	0.35 (0.26, 0.45) *	0.099
	PIP *cm H_2O*	13.8 (9, 19)	13.3 (9.7, 18)†	0.542
	Changes in FiO_2		-0.01 (-0.05, 0)	
	Changes in PIP *cm H_2O*		-0.2 (-1.5, 1)	
PDPV Group n = 30	FiO_2	0.4 (0.28, 0.6)	0.35 (0.3, 0.45)	0.074
	PIP *cm H_2O*	15 (10.5, 19)	13.4 (9.9, 18)	0.465
	Changes in FiO_2		0 (-0.1, 0)	0.980‡
	Changes in PIP *cm H_2O*		0 (-0.3, 0)	0.845‡

Normality test failed, Wilcoxon Signed Rank test is used
Values are expressed as median (25^{th}, 75^{th} percentiles)
* Including 1 missing value
† Including 2 missing values
‡ Mann-Whitney Rank Sum test is used
PIP = Peak Inspiratory Pressure

5.6 Haemodynamic changes

Haemodynamic data were collected immediately before and during treatment. The data collected included: systemic arterial blood pressure measured via an umbilical catheter or peripheral arterial line, heart rate (Hewlett Packard model 66S, Mennen Medical Inc. Horizon 2000, SpaceLabs Medical Infant Monitor), and oxygen saturation (Nellcor pulse oximeter). The "during treatment" values were the recordings that had the largest deviation from the pre-treatment baseline among all the recordings observed during the course of treatment. The results are summarised in Table 5.14. The difference of each parameter from the pre-treatment baseline was also compared between the two groups (Table 5.15). In order to exclude the adverse effect caused by suctioning procedures, all data did not include changes during suctioning.

In both groups, the "during treatment" values of all the parameters except SaO_2 were significantly different from their respective pre-treatment values. For all the parameters, the deviations of the "during treatment" values from the pre-treatment values were not significantly different between the two groups.

Comparison of the occurrence of adverse events during treatment (bradycardia: HR < 100 bpm; desaturation: SaO_2 < 80% requiring hand ventilation; drop in mean blood pressure > 5 mmHg) showed no significant difference between two groups (Table 5.16).

In both groups, pulmonary haemorrhage, pneumothorax, or other air leak syndromes were not observed in any of the infants.

Table 5-14 *Comparison of haemodynamic parameters Pre-treatment and maximal change during treatment*

		pre	during	*p* value
LST Group n = 26	Heart rate	157 ± 11	164 ± 17	<0.001
	SBP	57 ± 15	66 ± 15	<0.001*
	DBP	36 ± 11	41 ± 10	0.015*
	MBP	44 ± 12	52 ± 12	<0.001*
	SaO_2	95 (94, 97)	95 (94, 96)	0.583†
PDPV Group n = 30	Heart rate	155 ± 12	169 ± 15	<0.001
	SBP	52 (44, 59)	60 (50, 70)	<0.001‡
	DBP	31 (25, 37)	38 (29, 45)	<0.001‡
	MBP	40 (33, 46)	47 (38, 56)	<0.001‡
	SaO_2	94 (93, 96)	94 (91, 96)	0.039

Heart rate value are measured by beat per minute, SBP= Systolic blood pressure, DBP= Diastolic blood pressure, MBP= Mean blood pressure, all blood pressure units are measured in mmHg, SaO_2 = Oxygen saturation in percentage

*Including 5 missing value, † Including 4 missing values, ‡ Including 3 missing values

When Normality test failed, Wilcoxon Signed Rank test is used.

Values are expressed as median (25^{th}, 75^{th} percentiles)

When Normality test passed, paired t-test is used. Values are expressed as mean ± SD

Table 5-15 *Maximum deviation from pre-treatment haemodynamic parameters Comparison between LST and PDPV group*

	LST Group n=26	PDPV Group n=30	*p* value
Heart rate (beat/min)	9 (5, 15)	14 (6, 22)	0.079
SBP	8 (5, 14) *	8 (6, 15)‡	0.685
DBP	5 (3, 11) *	6 (4, 11)‡	0.596
MBP	7 (4, 12) *	6 (5, 14)‡	0.755
SaO_2	0 (-1, 2)†	0 (0, 0)	0.207

*Including 5 missing value, † Including 4 missing values, ‡ Including 3 missing values
Normality test failed, Mann-Whitney Rank Sum test is used
Values are expressed as median (25^{th}, 75^{th} percentiles)
When Normality test passed, unpaired t-test is used. Values are expressed as mean ± SD

Table 5-16 *Adverse events during treatment Comparison between LST and PDPV Group*

	LST Group n=26	PDPV Group n=30	*p* value
Mean Blood Pressure Drop ≥ 5 mmHg	3	4	1.00
Persistent bradycardia and desaturation requiring hand ventilation	2	2	1.00

Fisher Exact test is used

5.7 Arterial blood gas

Arterial blood gas values before and after first treatment were collected and consisted of: pH, PaO_2, $PaCO_2$, base excess. Only those data collected within three hours before and after treatment were used for analysis. The results were summarised in Table 5.17. The deviation of the post treatment blood gas parameters from their respective pre-treatment values were also compared (Table 5.18). None of the above comparisons showed any significant difference.

Table 5-17 *Comparison of arterial blood gas values: pre-treatment and post treatment*

		pre	post	*p* value
LST Group n=26*	Arterial pH	7.37 ± 0.12	7.37 ± 0.16	0.683
	PaO_2 (kPa)	7.19 ± 2.05	7.60 ± 2.28	0.505
	$PaCO_2$ (kPa)	5.73 ± 1.47	5.13 ± 3.06	0.441
	Base Excess (mmol/L)	-1.4 ± 5.5	-2.3 ±5.5	0.224
PDPV Group n=30†	Arterial pH	7.32 ± 0.05	7.32 ± 0.08	0.824
	PaO_2 (kPa)	8.54 ± 2.15	8.83 ± 1.70	0.599
	$PaCO_2$ (kPa)	5.71 ± 0.97	5.82 ±1.20	0.732
	Base Excess (mmol/L)	-3.4 (-5.9, -1.6)	-3.6 (-6.1, -1.6)	0.747

*Including 14 missing value, † Including 11 missing values
When Normality test passed, paired t-test is used. Values are expressed as mean ± SD
When Normality test failed, Wilcoxon Signed Rank test is used.
Values are expressed as median (25^{th}, 75^{th} percentiles)

Table 5-18 *Deviation from pre-treatment arterial blood gas values after first treatment Comparison between LST and PDPV group*

	LST Group n=26*	PDPV Group n=30†	*P* value
Arterial pH	0.00 ± 0.09	0 00± 0.08	0.781
PaO_2 (kPa)	0.38 ± 2.00	0.27 ±2.22	0.893
$PaCO_2$ (kPa)	-0.59 ± 2.57	0.11 ± 1.32	0.303
Base Excess (mmol/L)	-0.9 ± 2.5	0.1 ± 2.3	0.256

*Including 14 missing value, † Including 11 missing values
Normality test and equal variance test passed, unpaired t-test is used. Values are expressed as mean ± SD

5.8 Other clinical outcome

5.8.1 Bronchopulmonary dysplasia

The long term outcome in infancy is not within the scope of this study. We compared the duration of ventilation, duration of oxygen dependency and the occurrence of BPD between the two groups. Results are summarised in Table 5.19 and 5.20.

The number of infants successfully extubated and successfully weaned off oxygen showed no difference between the two groups. Mean value of mechanical ventilation days was smaller in the PDPV group, median duration of oxygen dependency was less for the LST group. These difference was however not statistically significant.

Occurrence of BPD showed no difference between the two groups.

Table 5-19 *Duration of mechanical ventilation and oxygen dependency Comparison between LST and PDPV group*

	LST Group n=26	PDPV Group n=30	*p* value
Infants successfully extubated	21	20	0.376*
Duration of Mechanical ventilation (days)	31 ± 28	23 ± 15	0.241†
Infants successfully weaned off oxygen	19	19	0.623*
Duration of oxygen dependency (days)	25 (9, 63)	34 (11, 42)	0.815‡

* Chi-square test is used.
† Normality test passed P = 0.059, equal variance test passed $p = 0.061$, unpaired t-test is used. Values are expressed as mean ± SD
‡ Normality test failed p=<0.001, Mann-Whitney Rank Sum test is used. Values are expressed as median (25^{th}, 75^{th} percentiles)

Table 5-20 *Occurrence of Bronchopulmonary Dysplasia Comparison between LST and PDPV group*

	LST Group n=26	PDPV Group n=30	*p* value
Infants diagnosed with BPD	13	13	0.818*

Chi-square test is used: Chi-square = 0.053, DF = 1

5.8.2 Intra-ventricular haemorrhage (IVH)

During the study period, incidence of grade three and four IVH, cystic lesions, and extension of the brain lesion, as confirmed by ultrasonography were compared between the two groups. Distribution of IVH in the two groups before and after intervention are summarised in Fig 5.11. Progression of IVH are summarised in Table 5.21.

In the LST group, there were five infants progressed from Grade 0-2 to Grade 3-4 IVH. In the PDPV group, seven infants presented with a similar pattern. The observation in the PDPV group was significantly different from what was expected from random occurrence ($p = 0.023$). There was no significant difference in the occurrence of cystic brain lesions between the two groups (Table 5.22). Some of the demographic characteristics of the infants presenting with cystic brain lesions after commencement of treatment are presented in Table 5.23.

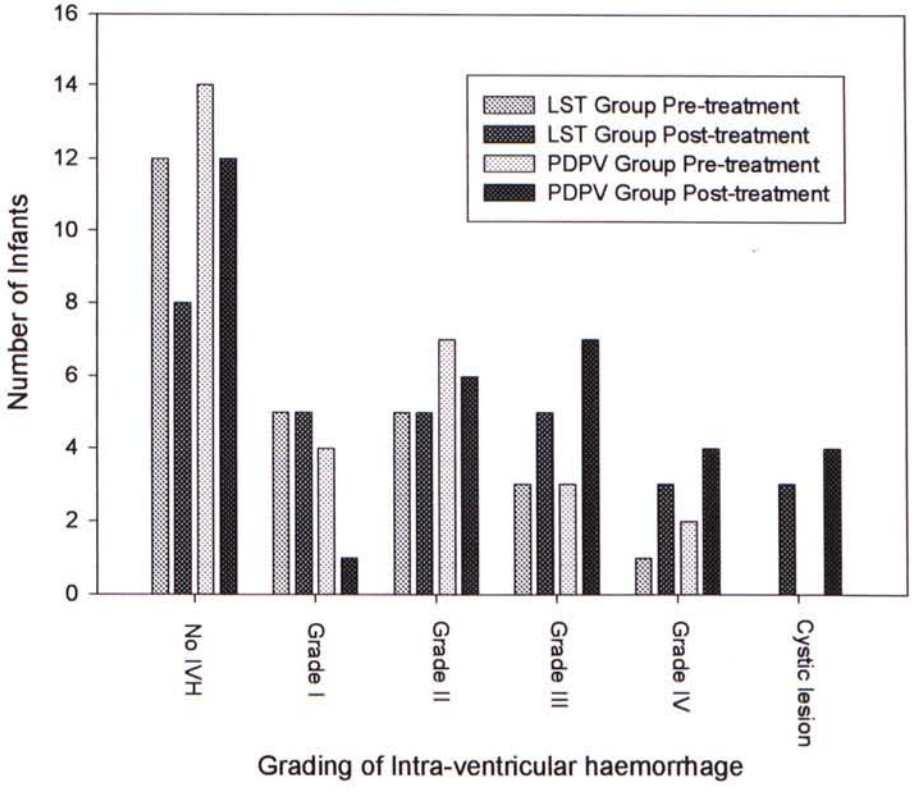


Figure 5-11: Distribution of intra-ventricular haemorrhage and cystic brain lesions

Pre and post-treatment distribution in LST and PDPV Groups are shown.

Table 5-21 *Incidence of intra-ventricular haemorrhage Comparison between LST and PDPV group*

	LST Group n=26		
Pre-therapy	Post-therapy		
	Grade 0-2	Grade 3-4	
Grade 0-2	18	5	
Grade 3-4	0	3	
Statistics	Chi-square=3.200	DF=1	*p*-value =0.074

	PDPV Group n=30		
Pre-therapy	Post-therapy		
	Grade 0-2	Grade 3-4	
Grade 0-2	18	7	
Grade 3-4	0	5	
Statistics	Chi-square=5.143	DF=1	*p*-value =0.023

* McNemar's test with Yates correction for continuity is used.

Table 5-22 *Occurrence of cystic brain lesions*
Comparison between LST group and PDPV group

	LST Group	PDPV Group	*p* value
	n=26	n=30	
Infants diagnosed with cystic brain lesions	3	4	1.000*

* Fisher Exact test is used.

Table 5-23 *Demographic characteristics of infants presenting with cystic brain lesions after start of treatment*

Subject	Gestational Age	Body weight	Outcome	Nature of lesion	Grading of Associated IVH	Diagnosed after initial treatment
	week	*g*				*days*
LST Group						
1	24.4	680	Died	(L) Subependymal cyst	2	2
2	29.4	1340	Alive	(L) Subependymal cyst	3	30
3[†]	25.7	690	Died	Multiple cystic areas	4	9
PDPV Group						
4	27	1150	Died	Cystic changes	2	64
5	23.9	550	Died	Periventricular cyst	3	22
6	26.9	910	Alive	Cystic changes	3	2
7	26.4	700	Alive	(L) Subependymal cyst	4	13

5.8.3 Mortality rate

The LST group had a lower mean mortality rate (31%) than that in the PDPV group (43%). The difference was however not statistically significant ($p = 0.489$, Chi-square test).

Part III Effects of Lung Squeezing Technique on Lung Mechanics

6. Chapter 6 Lung mechanics study for neonates

The purpose of this observational study was to assess the effects of LST on lung mechanics (respiratory system compliance [C_{rs}], and respiratory system resistance[R_{rs}]) of ventilated preterm infants.

A computerized data acquisition system (Model 2600 Pediatric Pulmonary Function Laboratory system, Sensormedics, Anaheim, CA) was used for assessment of C_{rs} and R_{rs} It utilizes a single breath occlusion technique that takes advantage of the influence of the Hering-Breuer inflation reflex (HBIR) on infants (Stocks et al 1996). Relaxation of the respiratory system is induced during a brief end-inspiratory airway occlusions. The passive expiratory flow is measured with a pneumotachograph (dead space 1.8 ml) after removal of the occlusion. Calculation of C_{rs} and R_{rs} is based on the passive flow-volume curve (Figure 6.1). Two assumptions are made for the measurement: (1) The Hering-Breuer reflex induced by occlusion leads to total relaxation of the muscles of breathing during the occlusion and throughout the subsequent expiration (2) Complete equilibration of pressure occurs throughout the lungs so that pressure measurement at the airway opening is equal to elastic recoil pressure of the respiratory system (Mortola 1994). The validation of single breath occlusion technique has been published by Lesouef and colleagues (1984) and provided quick and accurate measurements of respiratory mechanics.

This method measures the total compliance of the respiratory system (C_{rs}), which comprises the compliance of lung (C_L) and chest wall (C_W) represented by the equation:

$$1/ C_{rs} = 1/C_L + 1/C_W$$

Compliance refers to the distensibility or stretchability of the lungs and chest wall. This is defined as the change in lung volume in response to a change in transpulmonary pressure. Reduced distensibility of the lungs occurs in abdominal distension (interference with diaphragmatic movement), in lung disease (pulmonary congestion and fibrosis). Reduced chest wall distensibility is associated with the chest wall movement mechanics (stiffness, structural chest wall deformity). C_L and C_{rs} reach their highest values when alveolar units are maximally recruited, serial changes will reflect the changes in the lung mechanics after a treatment intervention. C_{rs} is affected by tissue elastance, size of the alveolar compartment and position on the pressure-volume curve. Both the relative compliances of the lungs and the chest wall (C_W) are contributing to the C_{rs}. In infants, as the C_W is very high, the obtained value for C_{rs} approximates that of lung compliance (Hand 1993).

Respiratory system resistance is a combination of airway resistance and pulmonary resistance. This denotes the frictional forces between gas flow and the airway and lung tissue. During positive pressure ventilation, gas flow occurs due to a difference between the pressure at the airway opening and alveolar pressure. This applied pressure is used to stretch the lung tissue and to overcome the resistance of the airways and lung tissues. Resistance of the respiratory system (R_{rs}) represents the sum of resistive properties of the airways, lung tissues, and chest wall as follows:

$$R_{rs} = R_{AW} + R_{tiss} + R_W$$

Measurement of R_{rs} by occlusion technique assesses expiratory resistance under passive conditions. Calculation of the time constant (τ_{rs}) is based on the expiratory slope of the passive expiratory flow-volume curve (Stocks et al 1996). Time constant indicates the rate of emptying of the lungs, based on calculation that 97% of the total volume is exhaled in 3 x time constant. It is affected by many factors, a long time constant may be caused by mucus obstruction, or increase in lung volume as the lung become more compliant.

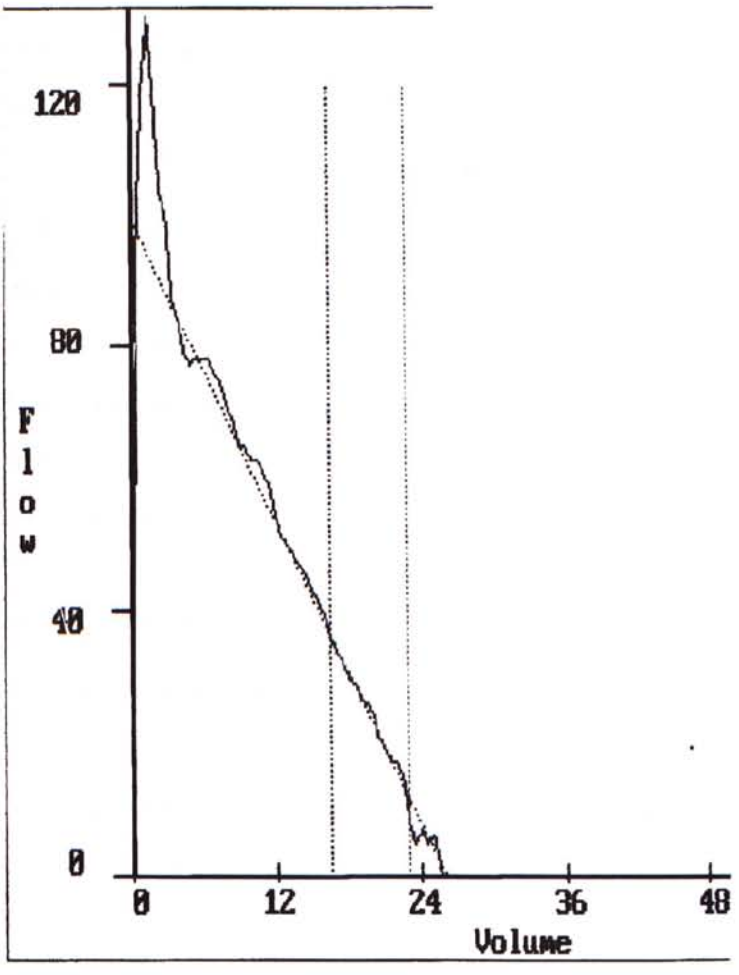


Figure 6-1 **Passive expiratory flow-volume curve obtained from the pneumotachograph**

The initial peak is artifact on release of the occlusion, the slanted dotted line represents the passive flow-volume relationship

6.1 Methods

Ventilated preterm infants were selected using the same inclusion criteria as the main study, except that the infants did not have lung collapse. The inclusion criteria were as follows: (1) Neonates with gestational age $\leq$ 37 weeks (2) Required ventilatory support (3) Absence of any segmental or lobar collapse confirmed on a CXR (4) Absence of major congenital malformation (5) Clinically and haemodynamically stable as determined by the attending neonatologist (6) No major airway interventions including change of endotracheal tube, hand ventilation or bronchial lavage had been performed in the previous 12 hours (7) The ventilator settings and FiO_2 had remained unchanged in the last 12 hours (8) Granting of parental consent

Assessment of the change in lung mechanics was performed based on a time series design. Endotracheal suctioning was performed to clear the proximal airway prior to each set of data collection. Measurement of lung mechanics was performed immediately before the lung squeezing procedure. Lung squeezing procedure and endotracheal suctioning were then performed in a manner as described in the main study. The amount of sputum collected in the suction catheter was measured using a 2.5 ml syringe. Post-treatment lung mechanics was measured immediately after the lung squeezing procedure, and repeated at four hours later to assess the carry over effect of the procedure.

All lung mechanics testing were performed at a specified time of the day: around 11:45a.m. (pre-treatment), 12:30a.m. (immediately post-treatment) and 16:30a.m. (4 hours post-treatment).

In each measurement, a total of 20 breaths was initially taken. A breath was accepted for analysis if the flow-volume curve satisfied the criteria as described by Popow et al. (1988) and Stocks et al. (1996): (1) the occlusion starting exactly at the end of an inspiration (2) a well defined pressure plateau of 0.1 s at end-inspiratory occlusion was achieved (3) The slope of the expiratory flow-volume loop appeared linear over at least 40% of the

expiration. All infants were studied at sleep state, tracings recorded during awake state or any agitated state were abandoned. From the 20 recorded breaths, at least 10 breaths with a coefficient of variation (SD ÷ mean) less than 10.0% were selected for analysis.

6.1.1 Statistical Analysis

Analysis of data was performed using One Way Repeated Measures Analysis of Variance (ANOVA) with Student-Newman-Keuls post hoc test for all pairwise comparison procedures. All data were checked for normality and equal variance test at alpha level 0.05. If any one test failed, Friedman Repeated Measures Analysis of Variance on Ranks test (RM ANOVA on ranks) was used for analysis. For all the data, differences were considered significant for rejection of the null hypothesis at $p < 0.05$. Data are expressed as mean ± SD.

Data from infants with or without obvious secretions were analysed separately. Secretions were defined as obvious when the amount of sputum collected were more than 0.15 ml.

Data were also analysed by classified into a low and a high value subgroup based on the mean value.

6.2 Results

A total of 11 preterm infants were enrolled in the lung mechanics study. Their demographic characteristics were given in Table 6.1. All infants were diagnosed to have respiratory distress syndrome (RDS).

Raw data representing C_{rs} and R_{rs} changes in each infant were shown in Figure 6.2 and 6.7 respectively. There were four infants constituted the group with secretions.

Compare to the pre-treatment values, there was a significant increase in C_{rs}, both immediately and 4 hours after LST (Figure 6.3). When C_{rs} was adjusted by body weight, only the immediately-after-LST value showed significant changes (Figure 6.4). For infants without secretions, there was a tendency for compliance to increase immediately after LST (Table 6.2). Only the low compliance subgroup showed significant rise both immediately after and 4 hours after LST (Figure 6.5 & 6.6).

Mean R_{rs} as a group did not change significantly after LST. However, pronounced decrease in R_{rs} was observed in the subgroup of infants who yielded secretion after LST, both immediately and 4 hours after LST (Figure 6.8). Neither the low nor high resistance subgroup showed any significant alteration in R_{rs} after LST (Figure 6.9).

Table 6-1 *Demographic characteristics of infants recruited in Lung Mechanics Study*

Subject	Gestational Age	Body Weight	Apgar score at 1 min / 5 min	Age at recruit	Ventilator parameters: Fraction of oxygen (FiO_2)	Ventilator parameters: Peak Inspiratory pressure (PIP)	Diagnosis
	week	*g*		*days*		*cm H_2O*	
1	33.7	1765	7 / 9	3	0.21	17	RDS
2	31.0	1815	6 / 9	18	0.25	18	RDS
3	29.1	1120	8 / 10	5	0.30	25	RDS
4	30.7	1690	6 / 9	2	0.21	24	RDS
5	27.4	785	7 / 9	5	0.25	12	RDS
6	27.4	765	7 / 9	8	0.35	15	RDS
7	33.3	1695	8 / 10	26	0.21	15	RDS
8	27.9	895	1 / 4	2	0.21	11	RDS
9	29.6	1350	9 / 10	5	0.21	17	RDS
10	27.1	1110	6 / 8	13	0.21	13	RDS
11	29.6	850	5 / 9	28	0.21	18	RDS
Mean ± SD	29.7± 2.3	1258 ± 419			0.24 ± 0.05	16.8 ± 4.5	

Effect of lung squeezing technique on Compliance (C_{rs})

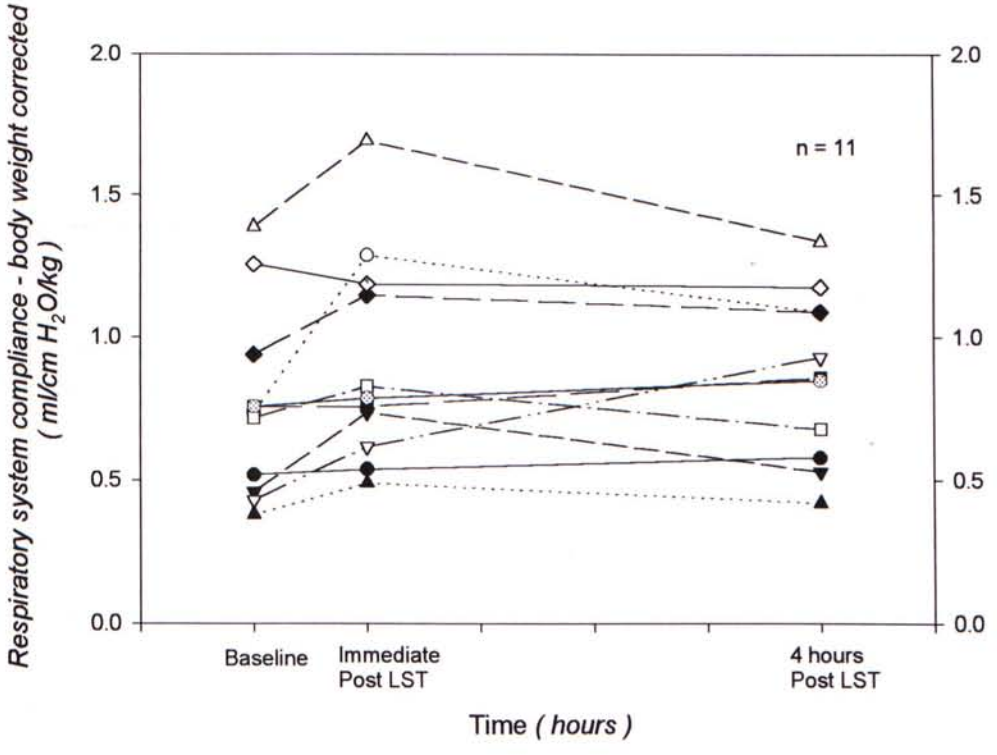


Figure 6-2: Respiratory system compliance (body weight corrected) Before, immediately after and 4 hours post LST Subjects representing by symbols ○ ▽ ◆ ◎ constituted the group with secretions

Table 6-2 *Mean(SD) respiratory system compliance*
Comparison before, immediately after and 4 hours after LST

Secretions obtained	Number of infants	Measurements before LST	Measurements immediate post LST	Measurements 4 hrs post LST	*p* value
		ml / cm H_2O			
O	7	0.82 ± 0.34	0.95 ± 0.37	0.85 ± 0.30	0.060
+	4	1.23 ± 0.58	1.72 ± 0.94	1.73 ± 0.66	0.094
Combined	11	0.97 ± 0.46	1.23 ± 0.71 *	1.17 ± 0.62 *	0.023 †

* $p < 0.05$

Values are expressed as mean ± SD
† Normality test failed, Friedman RM ANOVA on Ranks test is used

Table 6-3 *Mean (SD) respiratory system compliance (body weight corrected)*
Comparison before, immediately after and 4 hours after LST

Secretions obtained	Number of infants	Measurements before LST	Measurements immediate post LST	Measurements 4 hrs post LST	*p* value
		ml / cm H_2O / kg			
O	7	0.78 ± 0.40	0.89 ± 0.42	0.80 ± 0.35	0.093
+	4	0.72 ± 0.21	0.96 ± 0.31	0.99 ± 0.12	0.074
Combined	11	0.76 ± 0.33	0.92 ± 0.37 *	0.87 ± 0.29	0.023

* $p < 0.05$

Values are expressed as mean ± SD

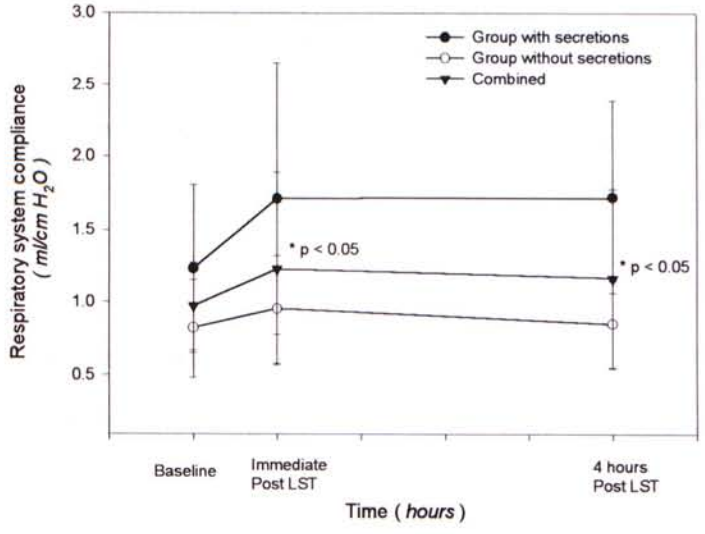


Figure 6-3: Mean respiratory system compliance Before, immediately after and 4 hours after LST

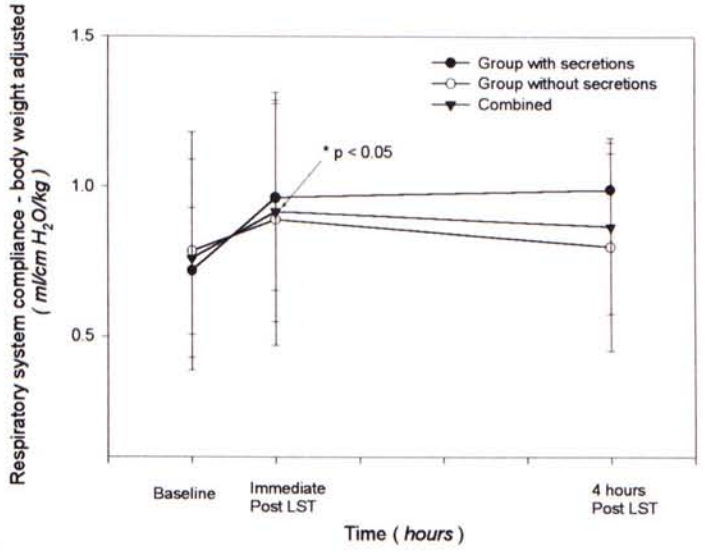


Figure 6-4: Mean respiratory system compliance (body weight corrected) Before, immediately after and 4 hours post LST

Table 6-4 *Mean (SD) respiratory system compliance*
Comparison before, immediately after and 4 hours after LST
High and low compliance group

Pre-treatment respiratory compliance	Number of infants	Measurements before LST	Measurements immediate post LST	Measurements 4 hrs post LST	*p* value
		ml / cm H_2O			
More than mean (0.97)	4	1.49 ± 0.32	1.95 ± 0.72	1.72 ± 0.61	0.141
Equal or less than mean	7	0.67 ± 0.14	0.82 ± 0.18 *	0.85 ± 0.36 *	0.021 †
Combined	11	0.97 ± 0.46	1.23 ± 0.71 *	1.17 ± 0.62 *	0.023 †

* $p < 0.05$

Values are expressed as mean ± SD
† Normality test failed, Friedman RM ANOVA on Ranks test is used

Table 6-5 *Mean (SD) respiratory system compliance (body weight corrected)*
Comparison before, immediately after and 4 hours after LST
High and low compliance group

Pre-treatment respiratory compliance	Number of infants	Measurements before LST	Measurements immediate post LST	Measurements 4 hrs post LST	*p* value
		ml / cm H_2O / kg			
More than mean (0.76)	3	1.20 ± 0.23	1.34 ± 0.30	1.20 ± 0.13	0.341
Equal or less than mean	8	0.60 ± 0.16	0.76 ± 0.25	0.74 ± 0.23 *	0.046
Combined	11	0.76 ± 0.33	0.92 ± 0.37 *	0.87 ± 0.29	0.023

* $p < 0.05$

Values are expressed as mean ± SD

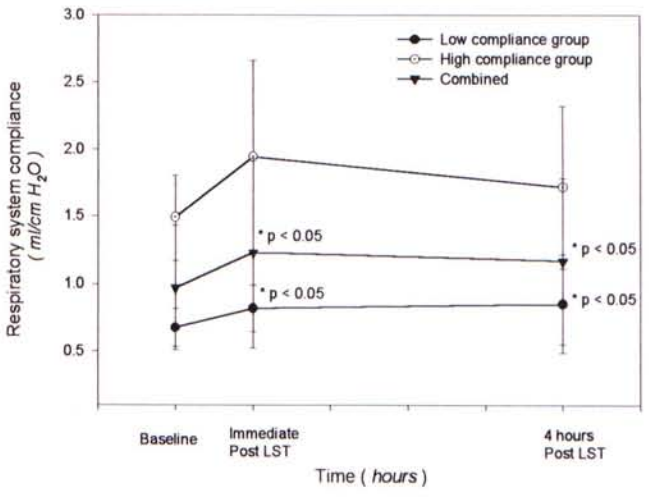


Figure 6-5: Mean respiratory system compliance in high and low compliance groups

Before, immediately after and 4 hours after LST

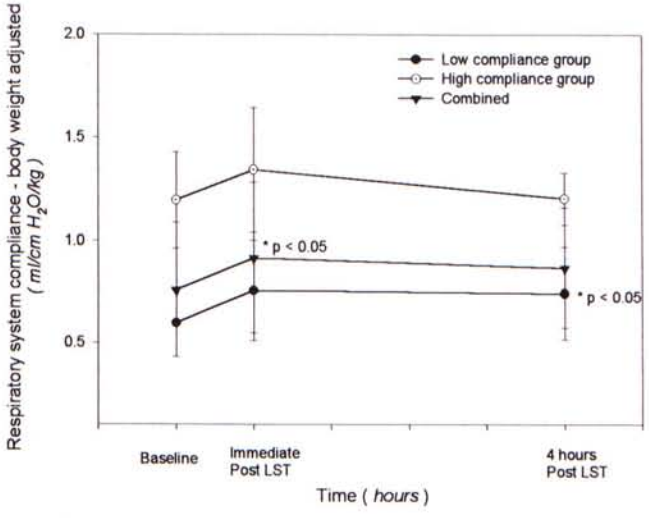


Figure 6-6: Mean respiratory system compliance (body weight corrected) in high and low compliance groups

Before, immediately after and 4 hours after LST

Effect of lung squeezing technique on Resistance (R_{rs})

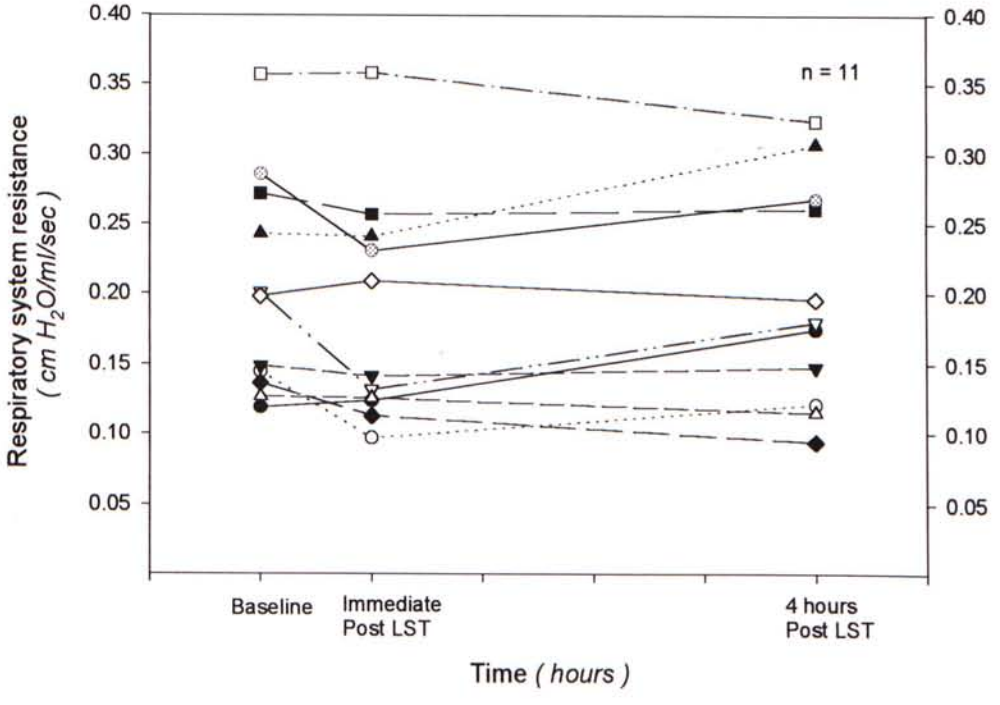


Figure 6-7: Respiratory system resistance
Before, immediately after and 4 hours post LST
Subjects representing by symbols ○ ▽ ◆ ◍ constituted the group with secretions

Table 6-6 *Mean (SD) respiratory system resistance*
Comparison before, immediately after and 4 hours after LST

Secretions obtained	Number of infants	Measurements before LST	Measurements immediate post LST	Measurements 4 hrs post LST	*p* value
		cm H_2O / ml / sec			
O	7	0.21 ± 0.09	0.21 ± 0.09	0.22 ± 0.08	0.648
+	4	0.19 ± 0.07	0.14 ± 0.06 *	0.17 ± 0.08 *	0.010
Combined	11	0.20 ± 0.08	0.19 ± 0.08	0.20 ± 0.08	0.147

* $p < 0.05$

Values are expressed as mean ± SD

Table 6-7 *Mean (SD) respiratory system resistance*
Comparison before, immediately after and 4 hours after LST
High and low resistance group

Pre-treatment respiratory resistance	Number of infants	Measurements before LST	Measurements immediate post LST	Measurements 4 hrs post LST	*p* value
		cm H_2O / ml / sec			
More than mean (0.20)	4	0.29 ± 0.05	0.27 ± 0.06	0.29 ± 0.03	0.584
Equal or less than mean	7	0.15 ± 0.03	0.14 ± 0.04	0.15 ± 0.04	0.275
Combined	11	0.20 ± 0.08	0.19 ± 0.08	0.20 ± 0.08	0.147

* $p < 0.05$

Values are expressed as mean ± SD

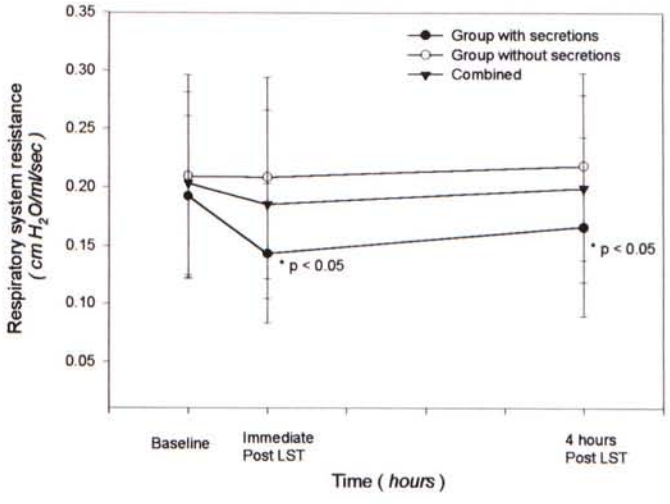


Figure 6-8: Mean respiratory system resistance Before, immediately after and 4 hours after LST

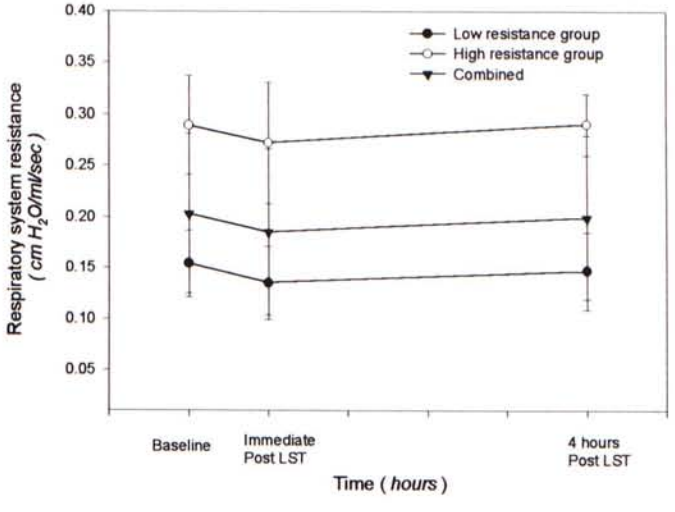


Figure 6-9: Mean respiratory system resistance in high and low resistance group Before, immediately after and 4 hours after LST

Part IV Discussion and Conclusion

7. Chapter 7 Summary and Conclusion

Lung atelectasis

Lobar atelectasis is a common form of atelectasis, and may affect any lobe. Eubanks and Bone (1990) categorised atelectasis in newborn into two main types: primary and secondary. Primary atelectasis is mainly caused by weak breathing effort and chest wall retraction in preterm infants. Secondary atelectasis is caused by aspiration of amniotic substance, mucus plugging, surfactant insufficiency or congenital malformation of the airways. Another form of plate atelectasis may occur in the form of flat, platelike densities (Miller 1997). Occasionally, recurrent lobar atelectasis is caused by endobronchial lesion (Nagaraj et al. 1980).

Delayed resolution of lung collapse will prolong the duration of mechanical ventilation and oxygen dependency. This findings of this study showed that infants treated with conventional physiotherapy technique required a larger number of treatment sessions to attain complete resolution of lung atelectasis (S_T) when compared to those treated by LST. However, the mean duration of mechanical ventilation and oxygen dependency between the two groups were not significantly different, suggesting that they were not affected by the choice of either LST or PDPV.

Efficacy of Lung Squeezing Technique

With either technique, first re-expansion of the atelectatic site was achieved within a short time after chest physiotherapy, as demonstrated in post-treatment chest X-ray. After the first treatment session, significantly more infants (81%) responded to LST as compared to

the PDPV group (23%). LST was more efficacious in reopening atelectatic lung than PDPV. The effect of either technique were not affected by the mode of ventilation, as within both groups, there was no difference in the rate of re-opening between the IPPV and HF subgroups.

Since the mode for number of treatment sessions to attain first re-expansion of lung atelectasis for PDPV group is two, we also compared the treatment response of both groups after completion of two treatment sessions. Significantly more infants (92%) responded to LST as compared to the PDPV group (60%). For slow or negative treatment response (unresolved cases), only 4% of the LST group required more than three sessions before first re-expansion occurred, whereas PDPV group had 30%, including 13% unresolved cases. This provided further evidence that LST was more efficacious in reopening atelectatic lung than PDPV.

Complete resolution of atelectasis without recurrence within three days was achieved in 10 infants (39%) in the LST group and, 4 infants (13%) in the PDPV group. The difference was however not statistically significant ($p = 0.059$). After stratification by the mode of ventilation, however it is evident that LST is more effective than PDPV in infants receiving IPPV ($p = 0.012$), but not in those receiving HF. Within the LST group, treatment sessions required by the IPPV subgroup was significantly smaller than that required by infants in the HF subgroup ($p = 0.031$), suggesting that efficacy of LST to attain total resolution of atelectasis is better in infants receiving IPPV. This discrepancy was not observed in infants treated with PDPV.

LST works by generating a pressure difference between the atelectatic lung segment and upper airway during the squeezing phase. This promotes removal of airway secretions. LST also increases transpulmonary pressure at the release phase of squeezing manoeuvre, which may enhance recruitment of the underventilated alveoli. As demonstrated in this study, these pressure changes are more effective in correcting lung atelectasis than the conventional PDPV technique.

Bias and Blinding

Prevention of selection bias was done by random assignment and blinding. Neonatologists referring neonates with lung atelectasis for physiotherapy had no knowledge about the study. Sample allocation into the experimental and control group was based on queue derived from a table of random numbers with stratification according to the mode of ventilation (conventional or high frequency). The gestational age and body weight between the LST and PDPV groups were similar.

The neonatologists responsible for analysis of chest X-ray result were blinded to the grouping of the infants. Members of the clinical team including paediatricians, nurses, and physiotherapists other than the investigator were blinded to the study.

Changes in lung mechanics post Lung Squeezing Technique

Physiotherapy with LST was followed immediately by a significant improvement in C_{rs}. The average increase was 21%. There was however little carry over effect as C_{rs} measured 4 hours post-treatment was not significantly different from the pre-treatment values.

Since most of the infants did not have significant secretion, removal of secretion could not have been responsible for the improvement in C_{rs}. We postulated that either *increase in alveoli recruitment* and/or the *reduction of airway closure* after LST had contributed to the increase in C_{rs}.

In order to investigate the efficacy of LST on infants with different levels of baseline compliance, we divided the infants into high and low C_{rs} subgroups based on the pre-

treatment mean C_{rs}. Significant improvement was observed in the low C_{rs} subgroup immediately and four hours post LST ($p = 0.046$), but not in the high C_{rs} subgroup. The better improvement in the low C_{rs} subgroup may be explained by the recovery of a larger number of atelectatic alveoli immediately post LST.

Mean R_{rs} changes as a group was not significant post LST ($p = 0.147$). However, in infants with significant airway secretion, there was a marked decrease in R_{rs} after LST ($p = 0.010$). Greatest drop of mean resistance value (26%) occurred immediately after LST ($p < 0.05$). This finding provided evidence that the improvement in R_{rs} was caused by the removal of secretion from the conducting airway.

Limitations of the study

Although the lung mechanics study gave supporting evidence for the efficacy of LST in correcting atelectasis, the sample size was small. Further investigation into changes in lung mechanics with a larger sample size may reveal more convincing data. We also made a clinical assumption that these lung mechanics changes happened in the process of resolution of lung atelectasis. However, the scope of this study did not look into the underlying mechanism of action of LST in correcting atelectasis.

Confounding factors

In the main study, confounding factors that could affect the resolution of atelectasis were excluded. Demographic characteristics and ventilator parameters of LST and PDPV groups were not significantly different. Factors that might affect removal or accumulation of bronchial secretion in the airways, including tracheal humidification, regular tracheobronchial suctioning and nursing routine on turning were common to both groups.

Prendiville and colleagues (1986) has shown that tracheobronchial suction caused significant fall in resistance. For the lung mechanics study, this confounding factor was eliminated since we performed suctioning prior to each set of data collection, so that the changes in resistance should be mainly contributed by LST. However, for the changes at 4 hours later, it was difficult to differentiate whether these changes were due to the carryover effect of LST or as a result of changes in the disease process. Therefore, we performed the lung mechanics study at a time that the ventilatory settings remained static within the past 12 hours, hopefully try to minimise the chance of clinical changes.

Interaction with ventilation mode

High frequency ventilation is a method of mechanical ventilation characterised by supraphysiological breathing rate, usually at the range of 10 to 15 Hz. Small tidal volumes are delivered with a positive inspiration, and active exhalation (in high frequency oscillatory ventilation). Mean airway pressure is often used as a strategy for maintaining lung volume. Despite the near-constant airway pressure characteristics of high frequency ventilation always keeps the lungs in an optimal lung volume, we are surprised to enroll a comparable number of lung atelectasis as that occurred in conventional ventilation. Although we speculated that mucus pooling was causing lung atelectasis, there were quite a considerable number of infants on high frequency ventilation presenting without obvious airway secretions (8 out of 15 in LST group, 9 out of 14 in PDPV group). There may be some other factors that are also contributing to lung atelectasis, these factors are also correctable by LST or PDPV. It may be that uneven distribution of ventilation due to alveolar instability may still occur in high frequency ventilation, thus contributing to the occurrence of lung atelectasis.

LST is derived based on a theoretical model of modified forced expiratory technique and augmented tidal volume. Airflow studies by Selsby and Jones (1990) did provide good evidence for forced expiratory technique in removal of the airway secretions. However, there was little literature support that the same phenomenon happened in high frequency mode. According to King and colleagues (1983), high frequency chest wall compression

enhanced tracheal mucus clearance. This was partly contributed by the higher peak expiratory flow at the air-mucus interface, and also due to the oscillation effect since the mucus clearance rate was also ventilator frequency-related, possibly caused by enhanced ciliary amplitude due to a mechanical resonance effect. Other oscillation effect brought reduced viscosity of sputum, possibly due to alteration of mucus crosslinking. In our main study, LST gave favourable results in attaining first re-expansion, in both IPPV and HF mode without significant difference ($p = 0.432$). However, for complete resolution of lung atelectasis, LST gave a better response in the IPPV mode when compared to HF mode ($p = 0.031$). It might be that high frequency ventilation was impeding some of the carryover effect of LST, although the underlying mechanisms remained unknown.

Secondary outcomes and adverse effects

The potential risk and the benefits of chest physiotherapy is always the prime interest of neonatologists and physiotherapists. In this study, all infants demonstrated haemodynamic changes including increase in heart rate, systolic, diastolic and mean blood pressure after LST or PDPV. The changes were similar between the two groups.

Changes in arterial blood gas were not significant in either group although there was an increase in PaO_2 and decrease in $PaCO_2$ in the LST group, and an increase in both PaO_2 and $PaCO_2$ in the PDPV group. Since we only evaluated post-treatment ABG after a stabilization period of at least 15 minutes, we made no attempt to compare the ABG results with those reported in previous studies. The immediate post-chest vibration drop in PaO_2 reported by Fox and colleagues (1978) might be a result of saline instillation and suctioning, rather than that of chest vibration. Finer (1978) measured ABG 15 minutes after percussion and PD, and reported an significant rise in PaO_2. We did not find a comparable increase in our PDPV group. In Finer's study, however, the treatment time (20 minutes) was longer than that in our study and the infants had larger birth weight (2072 g). Increase in PaO_2 after percussion or cupping was also reported by Tudehope and Bagley (1980).

Our findings also showed that the LST or PDPV groups did not differ in the duration of mechanical ventilation or oxygen dependency. The occurrence of BPD and mortality were also similar between the two groups. Long term neurological outcome was not evaluated in our study.

Selection of treatment techniques should always balance their efficacy and potential risks. We did not demonstrate any difference between the two groups in the occurrence of adverse events including major desaturation requiring hand ventilation, or drop in mean blood pressure by more than 5 mmHg. However, neonatologists and physiotherapists are most concerned about the potential association of physiotherapy with intra-cranial lesions. These are discussed in great details in the following paragraph.

Intra-ventricular haemorrhage

Although it was not a primary goal of this clinical trial, the results did allow us to examine the difference of occurrence and progression of intra-ventricular haemorrhage between the two groups of infants. There was a significant number of infants showing progression of Grade 0-2 IVH to Grade 3-4 after physiotherapy in the PDPV group ($p = 0.023$), but not in the LST group ($p = 0.074$). This finding should however be interpreted with caution because of the small sample size. Further research in this area is needed since inadvertent shaking of the head during physiotherapy may be responsible for the development and extension of IVH in preterm infants (Harding and Miles 1995).

Beeby and colleagues (1998) recently investigated the short and long term neurological outcomes following neonatal chest physiotherapy. Cystic brain injuries were noted at similar frequency in both physiotherapy (7%) and the non-physiotherapy group (5%). Furthermore, chest physiotherapy was not associated with any abnormal neurological outcomes. In our study, there was no significant difference in the occurrence of cystic brain lesions between the LST and PDPV groups.

Conclusion

In conclusion, lung squeezing technique (LST) is more effective in correcting lung atelectasis in ventilated preterm infants than the conventional postural drainage, percussion and vibration (PDPV) regimen. LST is superior to PDPV in achieving both first re-expansion and complete resolution of atelectasis, and is effective in infants ventilated by either high frequency or conventional ventilation. We observed no major adverse effects caused by LST, and there was no significant difference in haemodynamic disturbances when compared to PDPV. We found that the new technique did not reduce the incidence of BPD, cystic brain lesions, or overall mortality. It did not reduce the duration of mechanical ventilation or oxygen dependency, when compared to PDPV.

Based on the lung mechanics study, we postulate that LST promotes a stabilisation of the lung mechanics and causes re-expansion of lung atelectasis possibly through alveoli recruitment. LST also promotes airway patency by removing airway secretions. We conclude that lung squeezing technique is a safe, more effective volume recruitment manoeuvre in correcting lung atelectasis for preterm infants on mechanical ventilation, when compared to the conventional PDPV.

Part V Reference

8. BIBLIOGRAPHY

Alison J, Ellis E: Pulmonary function tests: Performance and interpretation In: Key Issues in cardiorespiratory physiotherapy. Butterworth-Heinemann Ltd 1992 (1st ed) 131-157.

Andersen JB, Qvist J, Kann T: Recruiting collapsed lung through collateral channels with positive end expiratory pressure. *Scan J Resp Dis* 1979; 60: 260-266.

Bailey C, Kattwinkel J, Teja K, et al.: Shallow versus deep endotracheal suctioning in young rabbits: pathologic effects on the tracheobronchial wall. *Pediatrics* 1988; 82(5): 746-751.

Bateman JRM, Newman SP, Daunt KM, et al: Regional lung clearance of excessive bronchial secretions during chest physiotherapy in patients with stable chronic airways obstruction. *Lancet* 1979; 2(10): 294-297.

Beeby PJ, Henderson-Smart DJ, Lacey JL, et al.: Short- and long-term neurological outcomes following neonatal chest physiotherapy. *J. Paediatr. Child Health* 1998; 34: 60-62.

Bertone N: The role of physiotherapy in a neonatal intensive care unit. *Australian J of Physiotherapy* 1988; 34(1): 27-34.

Bethune DD: Neurophysiological facilitation of respiration In: Respiratory care: International perspectives in physical therapy 7. Churchill Livingstone 1991 (1st ed) 121-145.

Boothroyd AE, Murthy BVS, Darbyshire A, et al.: Endotracheal suctioning causes right upper lobe collapse in intubated children. *Acta Paediatr* 1996; 85: 1422-5.

Brandstater B, Muallem M: Atelectasis following tracheal suction in infants. *Anesthesiology* 1969; 11: 468-473.

Chen CM, Tsai TC, Lan MC: Effect of body tilting on physiological functions in healthy term neonates. *Acta Paediatr* 1995; 84: 474-7.

Christensen EF, Nedergaard T, Dahl R: Long term treatment of chronic bronchitis with positive expiratory pressure mask and chest physiotherapy. *Chest* 1990; 97: 645-650.

Colbert D: Factors infuencing air flow In: The respiratory system In: Fundamentals of clinical physiology. (1st published) Prentice Hall International (UK) Ltd 1993a; 604-607.

Colbert D: Dynamic volume-pressure relationship: hysteresis loop In: The respiratory system In: Fundamentals of clinical physiology. (1st published) Prentice Hall International (UK) Ltd 1993b; 599-602.

Coney S.: News: Physiotherapy technique banned in Auckland. *Lancet* 1995; 345: 510.

Crane L: Physical therapy for neonates with respiratory dysfunction. *Physical Therapy* 1981; 61/12: 1764-1773.

Crane LD, Zombek M, Krauss AN, et al.: Comparison of chest physiotherapy techniques in infants with HMD. *Pediatric Research* 1978; 12(4): 559 (Abstract).

Cross JH, Harrison CJ, Preston PR, et al.: Postnatal encephaloclastic porencephaly - a new lesion? *Arch Dis in Childhood* 1992; 67: 307-311.

Cunningham ML, Nelson RM, Baun MM: The effects of inflation with two levels of supplemental oxygen during endotracheal suctioning of the premature neonate. *Pediatric research* 1983; 17(4): 310A (Abstract).

David A: Autogenic drainage - the German approach In: Respiratory care: International perspectives in physical therapy 7. Churchill Livingstone 1991 (1st ed) 65-78.

D'Souza SW, Janakova H, Minors D, et al.: Blood pressure, heart rate, and skin temperature in preterm infants: associations with periventricular haemorrhage. *Arch Dis in Childhood* 1995; 72: F162-F167.

Dezateux C, Stocks J: Lung development and early origins of childhood respiratory illness. *British Medical Bulletin* 1997; 53: 40-57.

Duara S, Bessard K, Keszler L, et al.: Evaluation of different percussion time intervals at chest physiotherapy (CPT) on neonatal pulmonary function parameters. *Pediatric Research* 1983; 17(4): 310A (Abstract).

Eckmann DM, Gavriely N: Chest vibration redistributes intra-airway CO_2 during tracheal insufflation in ventilatory failure. *Critical Care Medicine* 1996; 24: 451-457.

Etches PC, Scott B: Chest physiotherapy in the newborn: Effect on secretions removed. *Pediatrics* 1978; 62(5): 713-715.

Eubanks DH, Bone RC: Neonatal and pediatric respiratory care In: Comprehensive respiratory care: a learning approach 2nd edition. 1990; C.V.Mosby Company: 885-886.

Falk M, Kelstrup M, Andersen JB et al.: Improving the ketchup bottle method with positive expiratory pressure , PEP, in cystic fibrosis. *Eur J Respir Dis* 1984; 65:423-432.

Fanconi S, Duc G: Intratracheal suctioning in sick preterm infants: Prevention of intracranial hypertension and cerebral hypoperfusion by muscle paralysis. *Pediatrics* 1987; 79(4): 538-543.

Fewell J, Arrington R, Seibert J: The effect of head position and angle of tracheal bifurcation on bronchus catheterization in the intubated neonate. *Pediatrics* 1979; 64(3): 318-320.

Finer NN, Boyd J: Chest physiotherapy in the neonate: A controlled study. *Pediatrics* 1978; 61(2): 282-285.

Finer NN, Moriartey RR, Boyd J, et al.: Postextubation atelectasis: A retrospective review and a prospective controlled study. *J Pediatric* 1979; 94: 110-113.

Fisher DM, Frewen T, Swedlow DB: Increase in intracranial pressure during suctioning - stimulation vs rise in $PaCO_2$. *Anesthesiology* 1982; 57: 416-417.

Fox WW, Schwartz JG, and Shaffer TH: Pulmonary physiotherapy in neonates: Physiologic changes and respiratory management. *J Pediatrics* 1978; 92(6): 977-981.

Gerstmann DR, Minton SD, StoddardRA, et al: The Provo multicenter early high-frequency oscillatory ventilation trial: Improved pulmonary and clinical outcome in respiratory distress syndrome. *Pediatrics* 1996; 98(6): 1044-57.

Grosfeld JL, Lemons JL, Ballantine TVN, et al.: Emergency thoracotomy for acquired bronchopleural fistula in the preterm infant with respiratory distress. *J Pediatric Surg* 1980; 15: 416-421.

Groth S, Stafanger G, Dirksen H et al.: Positive expiratory pressure physiotherapy improves ventilation and reduces volume of trapped gas in cystic fibrosis. *Bull Eur Physiopathol Respir* 1985; 21: 339-343.

Halliday HL: Where are we now with the prenatal steroids and postnatal surfactant. *Biol Neonate* 1996; 69: 165-212.

Hand IL: Infant pulmonary function testing: Coming of age. *J for Respiratory Care Practitioners* 1993; 12(1): 83-90.

Harding JE, Miles FKI: In Proceedings of the Annual Scientific Meeting of the New Zealand Perinatal Society in conjunction with the Australian Perinatal Society, Thirteenth Annual Congress, Auckland, New Zealand 1995: A80; 169.

Hasani A, Pavia D, Agnew JE, et al.: The effect of unproductive coughing/FET on regional mucus movement in the human lungs. *Respiratory Medicine* 1991; 85(Suppl A):23-26.

Higgins RD, Richter SE, Davies MD: Nasal continuous positive airway pressure facilitates extubation of very low birth weight neonates. *Pediatrics* 1991; 88: 999-1003.

Imle PC: Percussion and vibration In: Chest physiotherapy in the intensive care unit (2^{nd} ed) Williams & Wilkins 1989; 134-152.

Javorka K, Tomori Z, Zavarska L: Mechanics of breathing during sneezing and crying in premature newborns. *Eur J Respir Dis* 1982; 63: 442-448.

King M, Phillips DM, Gross D, et al.: Enhanced tracheal mucus clearance with high frequency chest wall compression. *Am Rev Respir Dis* 1983; 128: 511-515.

King M, Phillips DM, Zidulka, et al.: Tracheal mucus clearance in high-frequency oscillation II: Chest wall versus mouth oscillation. *Am Rev Resp Dis* 1984; 130: 703-706.

Langston C, Kida K, Reed M, et al: Human lung growth in late gestation and in the neonate. *Am Rev Resp Dis* 1984; 129: 607-613.

Lesouef PN, England SJ, Bryan AC: passive respiratory mechanics in newborns and children. *Am Rev Respir Dis* 1984; 129: 553-556.

Lewis JA, Lacey JL, Henderson-smart DJ: A review of chest physiotherapy in neonatal intensive care units in Australia. *J Paediatr Child Health* 1992; 28: 297-300.

Light RW, George RB, Matthay MA, et al.: Mechanics of respiration In: Chest medicine: Essentials of pulmonary and critical care medicine (3rd ed) 1995, Williams & Wilkins. 43-62.

Lou HC, Lassen NA, Friis-Hansen B.: Is arterial hypertension crucial for the development of cerebral haemorrhage in premature infants? *Lancet* 1979; **I** : 1215-1217.

Macdonald A: Physiotherapy in the neonatal intensive care unit. *J of Canadian Physiotherapy Association* 1972; 24(2): 79-82.

Mackenzie CF, Shin B, McAslan TC.: Chest physiotherapy: The effect on arterial oxygenation. *Anesth Analg* 1978; 57: 28-30.

Mackenzie CF: Physiological changes following chest physiotherapy In: Chest physiotherapy in the intensive care unit (2nd ed) Williams & Wilkins 1989; 240-242.

McEvoy RD, Davies JH, Hedenstierna, et al.: Lung mucociliary transport during high-frequency ventilation. *Am Rev Resp Dis* 1982; 126: 452-458.

Menkes HA, Traystmen RJ :Collateral ventilation. *Am Rev Resp Dis* 1977; 116(2): 287-309.

Metlay LA, Macpherson TA, Doshi N, et al.: A new iatrogenic lesion in newborns requiring assisted ventilation. *N. Engl J Med* 1983; 309: 111-112.

Miller WT: The chest radiograph in the intensive care unit. *Seminars in Roent* 1997; XXXII: 89-101.

Morrell NW, Nijran KS, Biggs T, et al.: Regional matching of ventilation and perfusion during lobar bronchial occlusion in man. *Clinical Science* 1995; 88: 179-184.

Mortola JP: Neonatal respiratory mechanics in: Fetus and neonate: Physiology and clinical applications Vol 2: Breathing. (1st published) Cambridge University Press 1994 Ch.7:137-152.

Mupanemunda RH, Edwards AD: Treatment of newborn infants with inhaled nitric oxide. *Arch Dis in Childhood* 1995; 72: F131-F134.

Murray JF.: The Ketchup-bottle method. *N Engl J Med* 1979; 300:1155-57.

Nagaraj H, Shott R, Fellows R, et al.: Recurrent lobar atelectasis due to acquired bronchial stenosis in neonates. *J Pediatric Surg* 1980; 15: 411-5.

Nunn JF: Resistance to gas flow and airway closure In: Applied respiratory physiology Butterworths (3rd ed) 1987, 46-71.

O'Donohue WJ Jr: National survey of the usage of lung expansion modalities for the prevention and treatment of post-operative atelectasis following abdominal and thoracic surgery. *Chest* 1985; 87: 76-80.

Parker A: Chest physiotherapy in the neonate intensive care unit. *Physiotherapy* 1985; 71/2: 63-65.

Pedley TJ, Coriere P, Kamm RD, et al.: Gas flow and mixing in the airways. *Critical Care Medicine* 1994; 22, 9(Suppl.):S24-S35.

Placzek M, Silverman M: Selective placement of bronchial suction catheters in intubated neonates. *Arch Dis in Childhood* 1983; 58: 824-836.

Plessis AJ: Near-infrared spectroscopy for the in vivo study of cerebral hemodynamics and oxygenation. *Current Opinion in Pediatrics* 1995; 7(6): 632-9. (Abstract)

Portney LG, Watkins MP: Statistical measures of reliability In: Foundations of clinical research: Application to practice. Appleton & Lange 1993a (1st edition): 505-528.

Portney LG, Watkins MP: Power Analysis and determination of sample size In: Foundations of clinical research: Application to practice. Appleton & Lange 1993b (1st edition): 651-667.

Popow C, Simbruner G, Geubelle F: Respiratory compliance of healthy newborn infants measured by endinspiratory airway occlusion technique in the first hours of life. *Respiration* 1988, 53: 166-173.

Prendiville A, Thomson A, Silverman M: Effect of tracheobronchial suction on respiratory resistance in intubated preterm babies. *Arch Dis in Childhood* 1986; 61: 1178-1183.

Pryds O, Edwards AD: Cerebral blood flow in the newborn infant. *Arch Dis in Childhood* 1996; 74: F63-F69.

Pryor JA, Webber BA, and Hodson ME: Effect of chest physiotherapy on oxygen saturation in patients with cystic fibrosis. *Thorax* 1990; 45: 77.

Redding GJ: Atelectasis in childhood. *Pediatric Clinics of North Am* 1984; 31(4): 891-905.

Ross J, Dean E, Abboud RT: The effect of postural drainage positioning on ventilation homogeneity in health subjects. *Physical Therapy* 1992; 72(11): 794-799.

Runton N: Suctioning artificial airways in children: appropriate technique. *Pediatric* Nursing 1992; 18(2): 115-118.

Schürch S, Quanban R, Bachofen H, et al.: The surface-associated surfactant reservoir in the alveolar lining. *Biol Neonate* 1995; 67(suppl 1): 61-76.

Selsby D, Jones JG: Some physiological and clinical aspects of chest physiotherapy. *British J of Anaesthesia* 1990; 64: 621-231.

Shah AR, Kurth CD, Gwiazdowski SG, et al.: Fluctuations in cerebral oxygenation and blood volume during endotracheal suctioning in premature infants. *J Pediatr* 1992; 120: 769-74.

Simbruner G, Coradello H, Fodor M, et al.: Effect of tracheal suction on oxygenation, circulation, and lung mechanics in newborn infants. *Arch of Dis in Childhood* 1981; 56: 326-330.

Stocks J, Sly PD, Tepper RS, et al.: Passive respiratory mechanics In: Infant Respiratory function Testing. 1996 Wiley-Liss, Inc. 1st Ed. 283-327.

Sutton PP, Lopez-Vidriero MT, Pavia D, et al.: Assessment of percussion, vibratory-shaking and breathing exercises in chest physiotherapy. *Eur J Resp Dis* 1985; 66: 147-152.

Sutton PP, Parker RA, Webber BA, et al.: Assessment of the forced expiration technique, postural drainage and directed coughing in chest physiotherapy. *Eur J Resp Dis* 1983; 64: 62-68.

Sutton PP, Pavia D, Bateman JRM, et al.: Chest physiotherapy : a review. *Eur J Resp Dis* 1982; 63: 188-201.

Sykes K: Physiological background to mechanical ventilation In: Principles and practice series, respiratory support 1st edition BMJ Publishing Group 1995 Ch.2: 25-30.

Thomas J, Cook DJ, Brooks D: Chest physical therapy management of patients with cystic fibrosis: A meta-analysis. *Am J Resp Crit Care Med* 1995; 151: 846-850.

Tooley WH, Gregory GA: Treatment of the idiopathic respiratory distress syndrome in: Proceedings of a conference on the respiratory distress syndrome. 1973 Academic Press 357-367.

Touw TV, Tully A, Amis T, et al.: Cardiorespiratory consequences of expiratory chest wall compression during mechanical ventilation and severe hyperinflation. *Critical Care Medicine* 1993; 21: 1908-1914.

Tudehope DI, Bagley C: Techniques of physiotherapy in intubated babies with the respiratory distress syndrome. *Aust Paediatr J* 1980; 16: 226-228.

Tønnesen P, Støvring S: Positive expiratory pressure (PEP) as lung physiotherapy in cystic fibrosis. *Eur J Resp Dis* 1984; 65: 419-20.

Vaughan RS, Menke AJ, Giacoia GP: Pneumothorax: A complication of endotracheal tube suctioning. *J Pediatrics* 1978; 92(4): 633-634.

Verboon JML, Barker W, and Sterk PJ: The value of the forced expiration technique with and without postural drainage in adults with cystic fibrosis. *Eur J Resp Dis* 1986; 69:169-174.

Volpe JJ: Brain injury in the premature infant - current concepts of pathogenesis and prevention. *Biol Neonate* 1992; 62: 231-242.

Volpe JJ: Brain Injury in the premature infant: current concepts. *Biol Neonate* 1996; 69:165-212.

Wailoo MP, Emery JL: Normal growth and development of the trachea. *Thorax* 1982; 37(8): 584-7.

Wagaman MJ, Shutack JG, Moomjian AS, et al.: Improved oxygenation and lung compliance with prone positioning of neonates. *J Pediatrics* 1979; 94(5): 787-791.

Webber BA, Hofmeyr JL, Morgan MDL, et al.: Effects of postural drainage, incorporating the forced expiration technique, on pulmonary function in cystic fibrosis. *Br J Dis Chest* 1986; 80: 353-359.

Wetzel RC, Gioia FR: High Frequency Ventilation. *Pediatric Clinics of N Am* 1987; 34(1): 15-38.

Wyman ML, Kuhns LR: Lobar opacification of the lung after tracheal extubation in neonates. *J Pediatrics* 1977; 91: 109-112.

Zapletal A, Štefanová J, Horák J, et al.: Chest physiotherapy and airway obstruction in patients with cystic fibrosis - a negative report. *Eur J Resp Dis* 1983; 64: 426-433.

Part VI Glossary

This section provides a quick reference to some of the physiotherapy techniques or modalities mentioned in the background and chest physiotherapy chapters. References are cited by first author only. Complete bibliographic information is listed in the reference section.

Autogenic drainage Controlled breathing with varying rate and depth of respiration. Controlled mid-tidal breathing is followed by brief breath-holding at full inspiration. Relaxed and fast expiration to normal expiratory level, and then followed by forced expiration to a low expiratory reserve volume (for details, see David 1991)

Cupping Modified from of percussion by the use of various cup-shaped objects e.g. Bennett or Laderal resuscitation face mask (for details, see Tudehope 1980, Parker 1985, Bertone 1988)

Forced expiratory technique One or two forced huffs from mid-lung volume to low lung volume, often incorporated with self chest compression (for details, see Sutton 1983, Pryor 1990)

Intermittent Positive Pressure Breathing (IPPB) Use of pressure cycled machines e.g. 'Bird' respirator to deliver Intermittent positive pressure breathing (for details, see O'Donohue 1985)

Lung squeezing technique Three to four successive gentle and rhythmic squeezing of the chest wall in the range of expiratory volume followed by a quick release of the chest compression

PEP mask Positive expiratory pressure mask system consists of a face mask with a expiratory resistance valve (for details, see Falk 1984)

Percussion Clapping the chest wall in a rhythmic manner to produce an energy wave which is transmitted through the chest wall to the airways (for details, see Finer 1978, Crane 1981)

Postural drainage Positioning of body for bronchial drainage in gravity assisted positions based on the anatomy of the lobar bronchi which facilitate drainage of airway secretion from specific lung segments (for details, see Bateman 1979, Finer 1978, 1979, Crane 1978, Sutton 1983, Webber 1986)

Rib-springing Gentle 'springing' or squeezing of the rib cage at the end of expiration (for details, see Bertone 1988)

Shaking Coarse intermittent chest wall compressions applied during expiration

Vibration Intermittent chest wall compression incorporated with oscillatory movements delivered during expiration (for details, see Finer 1979, Crane 1981)

Part VII Appendices

CXR review for the evaluation of intra- and inter-rater reliability for the diagnosis of lung collapses

(The information will be used for the study of "Outcome evaluation of physiotherapy techniques for treating atelectasis")
Thank you for your assistance.

Q 1. Is there any lung collapse? Give ✓ for Yes(Y) or No(N)

Q 2. If there is lung collapse, where is the lobe/(segment) involved?

Sample Number	N	Y	Name lobe(s)/(segment) involved
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			
11			
12			
13			
14			
15			

Appendix II

OUTCOME EVALUATION OF CHEST PHYSIOTHERAPY

TECHNIQUES IN NEONATAL ICU (PWH)

NAME / HOSP NO DOB:	BIRTH HISTORY / DIAGNOSIS:

DATE / AGE BODY WT (Kg)	VENTILATOR MODE AND SETTING	AREA OF COLLAPSE	SEDATION / PARALYSED ABDOMINAL DISTENSION	BLOOD GAS PRE/POST (WITH TIME / NATURE)	V.S. BEFORE PHYSIO	MAP RANGE DURING PHYSIO	TIME FOR SaO_2 TO RECOVER POST PHYSIO	CXR / OTHER CLINICAL FINDINGS
DATE / AGE OTHER CONDITIONS							NAME OF PHYSIOTHERAPIST :	