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Lung function testing – useless in ventilated newborns?

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Abstract Several methods have been used for lung function testing in the ventilated newborn. The interest in the field has been stimulated by the recent appearance of commercially available equipment for assessment of mechanical parameters and of functional residual capacity in this group. Nevertheless, lung function testing is rarely used as a clinical routine, even such simple variables as tidal volume and minute ventilation. Among the many possible reasons for this condition, the fragile nature of the infants and the hands-off policy usually exercised, the difficulties in measuring flow accurately, and the complexity of the present methods deserve special attention. In order to change this situation more work needs to be done to elucidate basal physiology of the ventilated lung and the relationships between ventilator settings, lung function and side-effects in different conditions. If then sufficiently simple, safe and accurate methods to assess the most important functions can be offered, lung function testing would be likely to become a useful component of routine care in future neonatal intensive care.

Key words Infant newborn · Lung function testing · Mechanical ventilation

Abbreviations *BPD* bronchopulmonary dysplasia · *FRC* functional residual capacity · *IRDS* infantile respiratory distress syndrome · *PEEP* positive end expiratory pressure

Introduction

Different aspects of lung function have been measured in the ventilated preterm neonate. The minute ventilation achieved for a certain ventilator setting depends on the mechanical properties of the system. Static compliance depends on factors as functional residual capacity (FRC), lung water content, tissue elasticity and surfactant action. Dynamic compliance is, in addition, sensitive to flow distribution and visco-elastic properties of the respiratory system. Many factors determine the efficacy of gas mixing in health and disease, among them FRC, gas flow, and distal airway patency. Diffusion capacity and effective lung blood flow can be expected to change by numerous vasculatory and ventilatory factors such as lung water content, transpulmonary pressures, and vascular resistance.

Lung function testing now, by assessing such respiratory variables and parameters, has a potential value for the clinician by describing aspects of neonatal conditions quantitatively, and so demonstrate their pathophysiological profile and also reveal targets for therapeutic efforts. Lung function testing then has a role both for monitoring (to follow the course of disease, effect of treatments, and to guide ventilator settings) and for diagnostic purposes (classification, prognosis, choice of treatment).

Measurement of flow

Accurate measurement of ventilatory flow is central in most lung function tests. In intubated newborns, flow has usually been measured directly by means of a pneumotachograph [2, 28] or indirectly by means of a face-out body plethysmograph [11] or a jacket plethysmograph [27]. Pneumotachography close to the tube is simple to perform but the method is complicated by several problems. One is that conventional pneumotachographs small enough to fit in an intratracheal tube do not give linear output signals for the actual flow rates. Although this is a trivial problem to handle electronically, it is almost always solved by using larger pneumotachographs close to the tube connector which means increased dead space. Pneumotachographs are also sensitive to changes in gas composition and may also be inaccurate when used within a pressurized system [26]. The most serious problem, however, is that there is often a gas leak around the endotracheal tube. Such leaks are unpredictable and often difficult to detect and measure. If unnoticed, they will lead to an overestimation of the ventilatory flow. This problem may or may not be overcome by applying a gentle pressure onto the trachea. Tracheal pressure, however, changes the ventilation of the lungs and the measurement is not necessarily representative for the state before and after compression. If the leakage is small this error is limited and may be accepted for most purposes. It is doubtful, however, whether measurements should be done if leakage is present. These problems may be circumvented by use of a face-out body plethysmograph which can be designed for minimal disturbance of the infant and without any interference with the on-going ventilation [11]. The main disadvantage of this method of flow measurement is that it is more complicated to use and therefore not well suited for the clinical routine.

Airway pressure and gas sampling

Measurement of these modalities from the endotracheal tube is usually as simple in small neonates as in adults, provided the sampling flow is low. In ventilated individuals without spontaneous breathing, measurement of pleural and airway pressure gives the opportunity to study properties of the lungs and chest wall separately. The measurement of oesophageal pressure, however, is often inaccurate in these patients [21]. As the chest wall contributes little to the performance of the whole respiratory system in newborn infants, and particularly so in preterm infants [14], the properties of the lungs can be approximated by measuring over the whole respiratory system. For certain measurements an oesophageal recording can be of importance just to detect spontaneous breathing activity that might have disturbed the interpretation of a test result.

Concomitant dynamic measurement of flow and pressure is always difficult. Dissimilarities of the mechanical properties of the recording systems may induce considerable errors in the parameters calculated. This does not seem to be well known among users of commercial systems for assessment of dynamic lung mechanics. If, for example, a small piece of the pressure catheter is cut or the tubings to the pneumotachograph changed, the performance of the system may be severly damaged. The only way to handle this is to test the system for phase and amplitude shifts when driven with alternating flow with frequencies up to at least 10 Hz [23]. Such tests must be part of the routine if dynamic lung function tests are made.

Mechanics of breathing

If flow and pressure can be recorded accurately, the mechanical properties of the respiratory system can be assessed. Mechanical parameters can be expected to be informative about the state of large airways (resistance or conductance) and conditions that affect the recoil of the lungs (compliance or elastance). The most conventional lung model considers resistance and compliance to be linear over the breath and regards the applied airway pressure to be partitioned into one part proportional to the volume change with the inverse of compliance as parameter and another proportional to flow with resistance as parameter. The parameters may be estimated either by applying linear regression analysis after sampling of concomitant pressure and flow data over any part or the whole of a breath [23, 39] or by using zero flow and mid-volume data points only [25].

A more recent technique to assess these parameters in the same model is the occlusion method [16, 22]. This is based on the observation that, in spontaneous breathing infants, after a short airway occlusion, one part of the following expiration usually is passive and driven by elastic forces only.Then the flow – volume diagram is linear and its declination is determined by the time constant of the system which can be estimated from the graph. If, during repeated occlusions, the pressure in the airways of the relaxed respiratory system is also measured together with the corresponding volumes, the static compliance can be calculated separately. As compliance times resistance equals the time constant, the resistance parameter also can be assessed. In ventilated infants this method is even more simple to perform. Variants have also been used [30]. Different inflation techniques have also been presented. One requires constant inspiratory flow [36], another practices measurements between sequential, short inflations [22].

The advantage with the dynamic methods is that it can be used during ventilation and can be used continuously, if desired. A disadvantage is that matching of the recording systems is critical and that – in ventilated infants – spontaneous ventilation may interact which is difficult to

detect without a simultaneous oesophageal pressure recording. The occlusion method has the great advantage, in spontaneously breathing infants, that oesophageal pressure measurements are unnecessary and that it is insensitive to mismatch of the flow and pressure recording systems. It can be used also in infants without spontaneous ventilation after an inflation has been accomplished. Several studies have compared the different methods in use to assess the mechanical parameters [16, 19, 22, 30, 36]. Interestingly, the different methods seem to give comparable results.

A considerable body of experience with mechanical parameters in ventilated newborn infants has gathered. Dynamic compliance is very low in ventilated infants with infantile respiratory distress syndrome (IRDS) [10] compared to spontaneously breathing infants with the same condition [24]. It is also low in bronchopulmonary dysplasia (BPD) [17]. It may predict outcome in IRDS [18, 32] and in BPD [18]. It has also been reported that it does not predict the success of extubation [37] nor of surfactant therapy [40]. Neither does dynamic compliance indicate success of surfactant therapy during the first few hours in ventilated human infants [7, 9]. Lung compliance is dependent on lung size and must be normalised with body size or FRC before comparison between different infants can be made. The resistance of the system varies more within and between individuals than does compliance. One reason may be the endotracheal tube, where the flow usually is non-laminar and the resistance then flow dependent [35], and also dependent on tube length and degree of compression. Nevertheless, resistance has been reported to be high in BPD [15]. There is some controversy about the predictive power of an early observation of high resistance in ventilated infants [1, 17].

Lung volume and gas mixing

FRC has been assessed in ventilated as well as spontaneously breathing newborns by nitrogen dilution [5], helium dilution [20], nitrogen wash-out [29, 33] and recently also by a sulphur-hexafluoride wash-out method [38]. A tight endotracheal tube is essential for the gas dilution method to work and also for the wash-out methods which require the flow to be determined in addition to gas sampling facilities. A careful validation of each system by vessels with known volume is essential before any clinical use.

FRC may be used as a measure of lung size and thereby aid in the diagnosis of lung hypopasia which is an important differential diagnosis in the neonatal unit. However, a reduced FRC is also characteristic for IRDS [29] and there seems to be a close correlation between FRC and arterial oxygen tension in this condition, also after treatment with exogenous surfactant [9, 29]. One intention during mechanical ventilation of newborn infants is often to elevate the FRC. This is usually accomplished by applying PEEP. However, studies have shown that the effect of PEEP on FRC cannot be accurately predicted from compliance data in IRDS [8, 38]. Under certain conditions a short expiratory time may inadvertently lead to very high FRC with unfavourable effects on lung circulation [31]. These circumstances make FRC an important function to measure in the ventilated neonate.

The wash-out methods to measure FRC have an advantage in their potential to supply information also about the course of the wash-out, which may be interpreted in terms of gas mixing efficiency in the lung. This may be expressed as "lung clearance delay" [12], functional dead space [6] or as a nitrogen clearance index [34]. The gas mixing property has rarely been assessed in ventilated newborns with pulmonary disease, and has been reported to be impaired [10] or undisturbed [38] in ventilated preterm infants. It is likely that even small changes in the flow profile or in inspiratory and expiratory times may change the gas mixing property of ventilated lungs [4]. Consequently, gas mixing efficiency may be an important function to study in the future.

Effective lung blood flow and diffusion capacity

Although there are very few reports, these functions have been measured in ventilated newborns [3, 5, 13]. This requires a rebreathing system connected to the ventilator and tight-fitting endotracheal tubes. If multiple gases are used, FRC, effective lung blood flow and diffusion capacity can be measured at the same time. Recent studies with Doppler ultrasound technique [41] have confirmed the old observation that lung hypoperfusion is an essential feature of IRDS. Lung circulation is also affected by mechanical ventilation and it is very likely that monitoring of a measure of this function, together with others, would be an important tool to find optimal ventilator settings.

Conclusion

The main obstacle to useful lung function testing in the neonatal intensive care unit is our lack of knowledge on basic physiology of the sick, ventilated lung and the relationships between ventilator settings, lung function and side-effects in different conditions. When this situation improves and sufficiently simple, safe and accurate methods to assess the most important functions can be offered, lung function testing would be likely to become a useful component of routine care.

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