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Neonatal ventilation

Walid Habre, MD, PhD, Associate professor, Head Paediatric Anaesthesia Unit *

Geneva Children's Hospital, University Hospitals of Geneva, 6, rue Willy Donze, 1205 Geneva, Switzerland

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Preventing ventilation-induced lung injury and bronchopulmonary dysplasia is an important goal in the care of ventilated neonates. Recently, there have been tremendous efforts to improve ventilation strategies, which aim at ventilating with a 'protective' and 'open-lung' strategy. Several different ventilation modes are now available, but it is important to note that, with regard to the neonatal pulmonary and neural outcome, there is still no clear evidence as to the superiority of one ventilation mode over another. Clinicians should bear in mind that any ventilation mode used to ventilate a neonate should be accompanied by real-time pulmonary monitoring to continuously adapt the ventilation strategy to the sudden changes in the respiratory mechanical properties of the lung. This article will describe the different ventilation modes available for neonates and highlight the importance of using a protective and open-lung ventilation strategy, even in the operating room.

The past decade has seen a great increase in awareness of the potential harm of hyperventilation in neonates with large tidal volumes (V_t) leading to well-described ventilation-induced lung injury.[1,2] The mechanisms of this injury involve alveolar overdistension, the presence of shear forces and the release of pro-inflammatory cytokines. Moreover, inadvertent hyperventilation with consequent hypocapnia has been demonstrated to promote the development of cystic periventricular leukomalacia.[3] On the other hand, suboptimal V_t may result in inefficient gas exchange, hypercapnia, agitation and a potentially increased risk of intraventricular haemorrhage (IVH).[4] Thus, there have been extensive efforts to develop new ventilation strategies in neonates, based on non-invasive ventilation and the application of volume guarantee modes, to optimise V_t and to ventilate at optimal functional residual capacity

* Tel.: +41 22 3827 504; Fax: +41 22 38 25 485.
E-mail address: walid.habre@hcuge.ch.

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(FRC). Besides descriptions of the different ventilation modes available for neonates, this article will highlight the importance of using a ventilation strategy including low V_t, recruitment manoeuvres and high positive end-expiratory pressure (PEEP), especially in critically ill neonates.

Ventilation modes

Advances in ventilator technology have led to the development of various ventilation modes the usefulness of which has not yet been adequately proved either because of the lack of randomised trials and/or because studies have been done in heterogeneous groups. Although the terminology for the different ventilation modes used in neonates is confusing, these modes can be distinguished on the basis of whether they are volumetric (e.g., flow generator), barometric (pressure generator) or dual modes (combining pressure and flow generators). In addition, these modes can be either totally or partially controlled, with the child being able to trigger the onset of the ventilator cycle.

Pressure-controlled ventilation

This mode is often promoted in neonates in clinical practice since it provides a lower peak inspiratory pressure as a consequence of a limited and constant inspiratory pressure and a decelerating flow. The combination of decelerating flow and maintenance of constant airway pressure over time improves ventilation distribution, particularly in a lung with heterogeneous mechanical properties (as in acute lung injury), and thereby improves gas exchange.[5] Moreover, this mode allows compensation for a potential leak around an uncuffed endotracheal tube. The basic and most frequently applied mode in neonatal intensive care is 'the time-cycled, pressure-limited ventilation' (also called intermittent positive-pressure ventilation: IPPV). In addition to the limitation of the peak inspiratory pressure (PIP) and the level of PEEP, the settings for this mode require adjustment of the inspiratory (T_i) and expiratory time (T_e) to determine the respiration rate, irrespective of the child's own breathing, but usually at a level close to that observed physiologically. While ventilating with a short or a long T_i does not affect the incidence of chronic pulmonary disease (CPD) in neonates, there is some evidence that a short T_i duration is accompanied with decreased risk of air leak and a decreased mortality.[6] Thus, T_i is set between 0.35 and 0.5 s with a longer T_e unless a higher mean airway pressure is required, which can be achieved by elevating the PEEP level and/or reversing T_i/T_e. Nevertheless, this mode of ventilation often leads to an asynchrony between the child and the ventilator[7] and may result in the use of heavy sedation and neuromuscular blocking agents. Thus, synchronised ventilation with the patient allowed to trigger the onset of the ventilation is nowadays the common mode used in neonatal intensive care. Among the different triggering techniques that have been developed, flow triggering via a flow sensor interposed between the endotracheal tube and the ventilator's connection has been shown to be the most sensitive[8] and is therefore routinely applied in clinical practice. 'Synchronised intermittent mandatory ventilation' (SIMV) pressure control mode was the first mode in which the ventilator was set so as to secure a fixed respiration rate synchronised with the child's breathing within the limit of the ventilator setting. The ventilator does not assist a child breathing above this limit, but delivers additional untriggered cycles if the child is not breathing sufficiently to meet the predefined setting. For this reason, 'the assist-control' (AC) mode was developed in order to 'assist' each breath on the basis of positive-pressure ventilation, but with a 'control' of a minimum number of ventilator cycles. Nevertheless, if the child breathes at a high rate, the ventilator assists all triggered breaths by applying the initially set T_i, which will result in a decreased T_e and may lead to air trapping by shortening the time necessary to achieve adequate expiration. Accordingly, 'pressure support ventilation' (PSV) may be superior since both the initiation and the termination of ventilator assistance are controlled by the child's breathing effort and the changes occurring in the airflow. Depending on the ventilator, the inflation will stop when the inspiratory flow level decreases and reaches a percentage of the peak flow that varies between 10% and 25% of the maximum inspiratory flow.[9] Although PSV is associated with a lower work of breathing (WOB) and counteracts inadequate spontaneous breathing and the high resistance due to small endotracheal tubes, a novel technique called proportional assist ventilation (PAV) has been developed to reduce the WOB even further. In this mode, the rate of lung inflation and thus the inspiratory pressure are controlled by the patient and are proportional to the child's effort.[10]

Since the pressure applied depends on the inspiratory flow generated by the child, this mode assumes that the child is not hypopnaeic and there is no leak around the endotracheal tube.[7] More interesting is the neurally adjusted ventilator assist (NAVA), which relies on the child's respiratory control and diaphragmatic activity.[11] The inspiratory effort is detected via bipolar electrodes mounted on a naso-gastric feeding tube, positioned at the level of the diaphragm. The level of ventilatory support is then proportional to the inspiratory effort. While this mode is not affected by the presence of a leak, its utility is still not defined in neonates, especially in premature babies with immature control of the ventilation. A very recent prospective crossover study demonstrated that NAVA is associated with improved patient–ventilator synchrony and a lower peak airway pressure in comparison with PSV.[12]

Volume-controlled ventilation

Volume-controlled ventilation (VCV) is based on the traditional delivery of a fixed preset V_t at a pre-established rate. The major disadvantage of pressure-limited ventilation lies in the variable V_t that results from changes in lung compliance and resistance, as VCV does not take into account the pressure needed to deliver the desired V_t. Thus, high tracheal pressures may be encountered during ventilation, especially in the event of decreases in lung compliance or increases in airway resistance. These high pressures may be limited either by setting the pressure pop-off valve or by determining the level of T_i to limit high peak pressures during the ventilation of neonates with sick lungs. Nevertheless, this mode of ventilation is impractical and unpopular, particularly in infants, since the preset V_t is lost due to the compression of the gas in the ventilator circuit and to the leak around the uncuffed endotracheal tube.

Volume-targeted ventilation

The increasing awareness of the usefulness of direct control of the PIP and the benefit of ventilation with a small constant V_t led to the development of dual modes that guarantee V_t with a limited pressure.[13] Different ventilators and modes have been developed to enable the physician to choose a target V_t and set a high pressure limit that allows the ventilator to autoregulate the inspiratory pressure (within the maximum limit set) or the T_i to guarantee the target V_t. All these modes are grouped under the same terminology, recognised as 'volume-targeted ventilation modes', and include all modes that guarantee V_t by adjusting the inflating pressure in response to the exhaled V_t, which is compared with the desired target V_t.[14] However, there is still no evidence that volume-targeted ventilation offers any advantage over pressure-limited ventilation with regard to the outcome (death or the risk of CPD).[15] Nevertheless, volume-targeted ventilation has been associated with a significantly shorter duration of ventilation, a lower rate of pneumothorax and a decreased incidence of severe (grade 3 or 4) IVH relative to pressure-limited ventilation.[15]

The 'volume guarantee' (VG) ventilation mode is in fact a pressure-limited, volume-targeted time- or flow-cycled ventilator. This mode can be combined with all the other standard modes used in neonates, such as SIMV, AC or PSV. Besides the maximum PIP, the desired V_t (exhaled V_t) is set and also T_i, which determines the duration of insufflations. The ventilator bases its working pressure on the difference between the exhaled V_t and the desired V_t. However, adjustments in the working pressure are limited between one breath and another to avoid overinflating with high V_t, which reduces the risk of both volutrauma and barotrauma. Moreover, when the child triggers ventilation and/or lung compliance changes, the ventilator analyses each breath separately to maintain constant values for V_t. These characteristics are interesting during the weaning period since the inspiratory pressure is adjusted in real time.[13] The VG mode is far superior to 'volume-limited ventilation', which consists in setting an upper volume limit; if the measured inspired V_t exceeds this limit, the pressure support of the ventilator will stop. With this volume-limited mode, there is no automatic adjustment of the inspiratory pressure. In contrast, in the 'pressure-regulated volume control' (PRVC) mode, the flow rate will vary to adjust the inspiratory pressure to deliver the targeted V_t.[16] Thus, this mode behaves similarly to pressure control modes with regard to the pressure and flow patterns, but delivers the set V_t by adjusting the PIP on the basis of the lung compliance. This mode has been demonstrated in one study to be very useful in premature babies with very low birth weight (LBW) with a shorter duration of mechanical ventilation and less haemodynamic impairment.[17] When this mode is combined with

other ventilator options that allow the patient to breathe spontaneously with a pressure support, it is called 'automode'. The PRVC mode is more flexible than volume-assured pressure support ventilation (VAPS), which combines volume and pressure-targeted ventilation. The ventilator delivers the targeted V_t, but with a pressure-limited action in a pressure support mode. Since the pressure is limited, this mode acts by increasing the T_i, which may lead to expiratory asynchrony.

High-frequency ventilation

High-frequency ventilation (HFV) has rapidly come to the focus of interest in neonates since it allows ventilation with small tidal volumes and the application of a mean airway pressure (MAP) higher than that obtained with conventional ventilation. This strategy is very effective in infants with severe respiratory failure because HFV improves the gas exchange by optimising the lung volume while ventilating at lower proximal airway pressures and avoiding damage to the lungs.[18] The principle is based on the natural 'resonant' frequency of the lung and the fact that less pressure is required to move the gas into and out of the lungs at this resonant frequency, which is around 10 Hz (1 Hz = 60 bpm) in neonates and is even higher in premature babies. In fact, HFV improves the gas exchange by enhancing both the convection and the diffusion of the respiratory gases. Different ventilators delivering HFV are available and, despite the fact that they are of great value as a feature of the available modes of mechanical ventilation in neonates, there is no clear evidence in the literature as to the superiority of one type of HFV ventilator versus another. The first mode to be promoted was high-frequency jet ventilation (HFJV), a very well-established technique in the field of anaesthesia. It consists of delivering short bursts of gas (with very short T_i) at very high frequency (up to 600 min^{-1}) on top of a constant flow that determines a PEEP level. This technique necessitated a specific endotracheal tube, however, and failed to prove its usefulness in clinical practice, with conflicting results on the neurological and respiratory outcomes in neonates treated with this modality.[19–21] Another modality for the provision of HFV is high-frequency flow interruption (HFFI), which consists of interrupting at a high frequency (up to 20 Hz) a continuous flow delivered by a high-pressure gas source.[22] However, this technique failed to demonstrate any beneficial advantage as regards the pulmonary outcome, and some studies have even highlighted the higher incidence of air leaks in premature babies treated with HFFI.[23,24] The most frequently used modality nowadays is high-frequency oscillatory ventilation (HFOV). This modality is based on the presence of an electromagnetically driven piston or vibrating diaphragms that generate biphasic pressure waveforms at very high frequency (up to 15 Hz). Thus, HFOV has both an active inspiratory phase and an active expiratory phase (by inducing a negative proximal airway pressure during exhalation). When using HFOV, it is important to adjust the inspiration/expiration (I/E) ratio to avoid any gas trapping that may occur as a consequence of the active exhalation part.[9] HFOV provides very small oscillatory tidal volumes that are superimposed on an adjustable MAP. HFOV is, in theory, particularly beneficial when a high-volume strategy is required to maintain FRC as HFOV maintains FRC with a lower MAP than with other modes of ventilation. Nevertheless, a recent meta-analysis failed to demonstrate any evidence of a greater benefit of HFOV over conventional ventilation when used as a primary or rescue mode to ventilate infants with an acute pulmonary dysfunction.[25,26] There may be a lower incidence of chronic lung disease in premature babies ventilated with HFOV[26,27] but this finding needs to be confirmed in future trials.

Continuous positive airway pressure and non-invasive ventilation

The high incidence of complications following endotracheal intubation[28] and the concern about the potential harm of conventional ventilation led to the development of non-invasive respiratory support that allows the application of a continuous positive airway pressure (CPAP) and/or the delivery of non-invasive ventilation (NIV). Note that at least some CPAP is essential for recruiting, and maintaining airway patency and lung expansion.[29] The aim of nasal CPAP is to maintain FRC, decrease the WOB and reduce the frequency of apnoea of prematurity.[30] It is therefore routinely used in clinical practice to support recently extubated pre-term infants and, as an alternative to intubation and ventilation, to support those experiencing significant apnoea of prematurity and those with respiratory distress soon after birth. Some systems also allow the provision of a phasic positive increase in pressure (pressure

support or pressure-controlled) on top of the CPAP and can be synchronised (SNIMV, synchronised nasal intermittent mandatory ventilation) or not (NIMV). During the past decade, the use of NIV for acute respiratory failure in neonates has been expanding, and predictive factors for the successful use of NIV have recently been identified.[31] However, there are still no clear guidelines for the initiation of NIV. The main disadvantages of NIV are mainly based on the inability of NIV to oxygenate and ventilate the patient in a satisfactory manner despite the fact that NIV is well tolerated by the child. While meta-analyses have failed to demonstrate the benefit of NIV in the presence of respiratory distress syndrome,[32] its ability to prevent extubation failure in neonates is beyond doubt.[33] Accordingly, the use of NIV to protect against the risk of re-intubation during the first 72 h is the current evidence-based indication for NIV in neonates.[29] For this purpose, NIV is started after the minimal PEEP level is set to around 6-cm H_2O and the PIP to between 10- and 12-cm H_2O.

CPAP can be delivered essentially by two means: (1) a continuous flow and a device that varies the exhalation either by modifying the expiratory orifice size or by immersing the distal end under water to a certain level, which determines the desired CPAP. This latter is called 'bubble CPAP', the bubbles creating pressure oscillations that are transmitted to the airway opening, and it has been suggested that this phenomenon may improve gas exchange by facilitating diffusion.[34] (2) a variable flow that allows change of the CPAP level, but needs nasal prongs, which redirect the exhaled gas out of the expiratory limb. The WOB with the variable-flow CPAP has been shown to be less than that with the bubble CPAP.[35] Another system that is based on the variable-flow setting is the bilevel CPAP or BiPAP. The BiPAP allows the child to trigger the inspiratory phase and to breathe between two levels of positive pressure, with some systems including an abdominal wall sensor to help synchronisation with the child's inspiratory efforts. The BiPAP system seems to be better in improving oxygenation and ventilation than the CPAP system in LBW infants.[36]

The application and successful use of CPAP and NIV rely on the airway interfaces and their ability to guarantee comfort and optimise the delivery of pressure. Of all the interfaces that are available to provide CPAP, the binasal prongs have been demonstrated to be superior.[37] While prongs may be associated with a high incidence of nasal trauma in infants,[9] leaks remain a major concern in NIV. Such leaks may lead to reduced alveolar ventilation, child-ventilator asynchrony and increased nasal resistance.

Extracorporal membrane oxygenation (ECMO)

With the exception of heart failure, the use of ECMO in neonates is indicated when all modes of conventional ventilation (including HFOV and nitric oxide) have failed to maintain adequate oxygenation in the presence of reversible respiratory failure. Persistent pulmonary hypertension is a characteristic of nearly all diseases treated by ECMO (meconium aspiration, severe hyaline membrane disease, idiopathic persistent pulmonary hypertension, sepsis and congenital diaphragmatic hernia). The use of neonatal ECMO requires an experienced team that is at ease with the technique and can face all the complications related to its use in neonates. Due to the size of the cannula and the risk of IVH with heparinisation in the premature brain, neonatal ECMO can be considered only in neonates older than 34 weeks post-menstrual age and/or greater than 2 kg body weight. Under these conditions, the survival rate for neonates appears to be much higher than for either paediatric or adult patients.[38] However, intracranial injury continues to be a major complication associated with ECMO-treated neonates.[39] There are two potential ways to perform neonatal ECMO: veno-arterial or veno-venous ECMO. A total bypass, particularly in cases of associated heart failure, requires a veno-arterial technique where the venous cannula is inserted into the internal jugular vein and advanced through the superior vena cava, while the arterial cannula is placed into the right common carotid artery with the tip of the cannula advanced up to the innominate artery. In veno-venous ECMO, a double-lumen cannula is often used so that only one vessel is cannulated and the blood is drained from the right atrium, is oxygenated and is returned to the right atrium. Recent meta-analyses, including the four available trials in which ECMO was compared with conventional ventilatory support for severe respiratory failure, demonstrated the strong benefit of ECMO as concerns mortality (relative risk (RR) 0.44; 95% confidence interval (CI) 0.31–0.61), especially for babies without congenital diaphragmatic hernia (RR 0.33, 95% CI 0.21–0.53).[40] Nevertheless, further studies are needed to determine the criteria

for the introduction of ECMO, and long-term follow-ups are needed in view of the high incidence of severely disabled children.

Application of ventilation modes in the operating theatre

Despite the great advances in the development of new anaesthetic ventilators, which include a variety of modes of ventilation widely used in the intensive care setting, there is still no evidence as to the benefit of these modes of ventilation under general anaesthesia in improving the clinical outcome. However, the application of these modes to neonates helps the clinician to apply ventilation strategies that are part of the 'lung protective ventilation' and optimise the ventilation distribution. Since most of the neonates admitted to the operating theatre receive neuromuscular blocking drugs, mandatory ventilation is often used, while the synchronised ventilation mode is applied during induction or weaning from the ventilator (Table 1).

As stated above, the traditional mandatory VCV is inappropriate in the paediatric anaesthesia setting because it implies the use of a constant flow and it does not take into account the compressible volume and the potential air leak around the endotracheal tube. The constant flow characterising the VCV mode induces high PIP with less time for equilibrium to be attained between the airway (P_{aw}) and the alveolar pressure (P_{alv}), this being known as the time constant. Moreover, the compressible volume is an important issue in the neonate and it is crucial to know if the ventilator corrects for this compressible volume in the case of a fixed V_t setting. Most modern ventilators available in the anaesthesia setting do correct for this compressible volume when the ventilator is checked during the first use. If there is a change of circuits between patients, it is important to recheck the ventilator to correct for the compressible volume. In the event of an old ventilator or limited compensation if the pressure exceeds 30 cmH_2O,[41] it is important to take the compressible volume into account when

Table 1
Summary of different available modes of ventilation with their particular settings.

Mode of ventilation	Abbreviation	Settings
Pressure controlled ventilation	PCV	Set PIP and PEEP Set Rate independently from T_i and T_e
Intermittent positive-pressure ventilation	IPPV or time-cycled, pressure-limited ventilation	Limitation of PIP and PEEP Set T_i at 0.35 s. Rate depends on T_i and T_e
Synchronized intermittent mandatory ventilation	SIMV	Fixed respiration rate synchronized with child's breathing within limit of ventilator setting.
Assist-control	AC	Assist each breath on the basis of PCV Set minimum cycles and short T_i
Pressure support ventilation	PSV	Set variables for support based on PCV Set minimum rate and trigger threshold ± pressure slope
Neurally adjusted ventilator assist	NAVA	Set trigger to pick up the electrical diaphragmatic activity Adapt NAVA level to regulate pressure support
Volume-controlled ventilation	VCV	Fixed preset V_t and rate Limit high pressures with pop-off valve or T_i
Volume guarantee ventilation mode	VG or pressure-limited, volume-targeted time	Set the maximum PIP and PEEP, the desired exhaled V_t and T_i
Volume-limited ventilation	VLV	Set upper volume limit And Pressure support variables
Pressure-regulated volume control	PRVC or autoflow	Flow rate will vary to adjust PIP to deliver target V_t
Volume-assured pressure support	VAPS	Combines volume and pressure-target ventilation Set target V_t and Pressure limit as in PSV
High-frequency jet ventilation	HFJV	Short bursts with short T_i High frequency (600/min) constant flow determines PEEP level
High-frequency flow interruption	HFFI	Interrupts at high frequency (20 Hz) continuous flow
High-frequency oscillatory ventilation	HFOV	Adjust MAP, I/E ratio, Rate

PIP, peak inspiratory pressure; T_i, inspiratory time; T_e, expiratory time; MAP, mean airway pressure; V_t, tidal volume.

setting the V_t. For instance, if the compressible volume reaches 1 ml cmH_2O, and the delivered V_t is set at 7 ml kg^{-1} in a 3 kg neonate, the ventilator may generate a PIP of 25 cm H_2O during ventilation and thus have 25 ml of compressible volume. The preset V_t should be adjusted to almost 15 ml kg^{-1} because 50% or more may be lost in the delivery system (not taking into account the dead space and the potential leak). In any case, use of the VCV mode requires that the overpressure valve be set to protect the lung from any dangerous increase in peak pressure that may be induced by changes in lung compliance during the surgery. In neonates, therefore, particularly with a less compliant lung, the PCV is the mode of choice for ventilation.

The decelerating flow that characterises the PCV mode offers a limited and constant inspiratory pressure with a plateau pressure that is reached much more quickly, but at a lower PIP. This mode has been demonstrated to improve the ventilation distribution, decrease the intrapulmonary shunt and thus improve oxygenation. In addition, the PCV mode allows any compensation in the presence of a leak around the endotracheal tube. Nevertheless, while PCV better meets the criteria required by the protective ventilation strategy, V_t will be variable in this mode, particularly if there is a decrease in lung compliance or an increase in respiratory resistances during the surgery. During PCV, V_t is variable and depends on three components: (i) the time constant, (ii) the pressure gradient between the maximal set peak pressure and the PEEP level, and (iii) T_i, which is determined by the respiration rate and the ratio I/E. The time constant is characterised by the mechanical properties of the respiratory system, which include the total respiratory system compliance (Crs) and resistance (Rrs). Application of the time constant concept to the inspiratory phase implies that T_i is set to allow enough time for the achievement of pressure equilibrium between the airways and the alveoli. Accordingly, if Rrs increases and/or Crs decreases, the equilibrium time will increase. Further, it is important to allow sufficient time for complete deflation, considering that the expiratory flow presents an exponential decelerating profile and thus, almost three to four time constants of the respiratory system are needed for complete deflation. Finally, it is important to note that the available anaesthetic ventilators are not equal in generating a maximal insufflation flow, and the V_t generated by a given pressure level may vary from one ventilator to another.[42]

Given the benefit of maintaining diaphragmatic activity to decrease a ventilation perfusion mismatch during general anaesthesia, use of the PSV mode in routine practice is becoming very popular in paediatric anaesthesia. The new ventilators include a flow trigger highly sensitive to minimal flow variations (similar to those observed with intensive care ventilators) and can therefore be applied in neonates since minimal WOB is required to activate the beginning of the inspiratory phase.[43] The pressure support is based on a decelerating flow, which generates a fixed insufflation pressure; thus, V_t may vary with the patient's inspiratory efforts, the level of pressure support and also the mechanical characteristics of the lung. Currently, it is not possible to vary the cycling (transition from inspiration and expiration) on anaesthetic machines. In most ventilators, the insufflation stops when the flow is less than 25% of the maximal inspiratory flow. This limitation may have a negative impact in the presence of a neonate with an obstructive disease, where the cycling should occur later.[44] Although there have been no studies on use of the PSV mode in neonates, it can be applied during anaesthesia in clinical practice to compensate the increase in the WOB, which is particularly high in neonates. For instance, application of a pressure support of 5 cmH_2O in addition to a PEEP level at induction will help keep the airways patent, compensating the WOB; and it may ease inhalation induction by optimising the gas exchange. During the maintenance of anaesthesia, a higher level of pressure support may be necessary (up to 10 cmH_2O) to counteract the resistances due to the endotracheal tube and the circuit and to guarantee an optimal V_t for gas exchange.[45] At the end of an anaesthetic procedure, PSV allows a smoother recovery and weaning from the ventilator. In all cases, it is important to set a minimal security respiration rate to deliver in a pressure control mode in the event of apnoea. Finally, some anaesthetic ventilators allow changes in the pressure slope (the time to achieve pressure support). By increasing this time (and thereby decreasing the pressure slope), we can limit the auto-trigger activated by the cardiac activity, which is frequently observed in neonates at low trigger threshold.[46] To avoid this phenomenon, it is also possible to increase the trigger threshold with the risk of increasing the WOB.

Recently, the PRVC mode with automode (auto-flow) has become part of the new anaesthetic ventilators introduced in the operating theatre. VCV with decelerating flow in combination with synchronisation with a pressure support of the spontaneous ventilation offers the advantages of pressure modes, but with the guarantee of a minimal V_t. Theoretically, this mode overcomes the inconvenience of

both PCV and VCV and may have tremendous advantage in neonates under anaesthesia, particularly when abrupt changes in lung compliance occur during surgery (i.e., laparoscopy, or abdominal or thoracic surgery). Nevertheless, there are still no data concerning the use of this mode in the operating theatre and hence its use is still anecdotal and based on the experience of different clinicians.

'Open lung' and 'protective' ventilation strategy in the operating theatre

The open-lung strategy that is applied in the intensive care unit (ICU) should also be considered when a neonate is ventilated in the operating theatre. This strategy primarily targets the atelectasis and the consequent ventilation inhomogeneity observed under general anaesthesia, which can significantly impair the pulmonary gas exchange. First of all, the physiological characteristics of the chest wall (high compliance) and the lung (increased static elastic recoil pressure) in neonates promote airway closure and a decrease in FRC. The decrease in ventilation induced by general anaesthetics and the inactivation of the intercostal muscle activity associated with the cranial shift of the diaphragm are also responsible for the lung collapse and atelectasis formation. This latter is enhanced by the resorption of alveolar gas in the event of inhalation of a high FiO_2 concentration. Thus, this 'open-lung strategy' requires that recruitment manoeuvres should be regularly performed, such as application of a vital capacity manoeuvre (or twice the V_t) after induction, after disconnection and suction, and thereafter every 30 min during the anaesthetic procedure.[47] However, and in all cases, a minimum PEEP level of 5 cmH_2O is required to maintain recruitment of the distal airways[48] and the use of high concentrations of oxygen should be avoided. Nevertheless, a higher PEEP may be required in the presence of poorly compliant and atelectatic lungs to maintain adequate alveolar recruitment.

In addition to this open-lung strategy, it is crucial to apply 'protective ventilation' in an attempt to protect against ventilator-induced lung injury.[49] Ventilation with low V_t at optimal FRC is therefore also essential in the operating theatre. Optimisation of the PEEP level will increase the lung volume while adapting T_i and T_e, will guarantee adequate lung inflation and deflation, respectively, especially if T_i/T_e is adjustable on the basis of estimations of the time constants.

This ventilation strategy may lead to mild hypercapnia, which can be regarded as safe if maintained at around 6–7 kPa in the absence of high intracerebral pressure and pulmonary hypertension. It has also been demonstrated that mild hypercapnia at this level improves both the cerebral oxygen saturation and the subcutaneous tissue oxygenation.[50] Paediatric anaesthetists should be more aware of the importance of the position of the oxygen–haemoglobin dissociation curve. The large affinity for oxygen of foetal haemoglobin in comparison with that in the adult explains the shift of the curve to the left with a very low P_{50}, which can be aggravated in cases of hyperventilation (Bohr effect) with a subsequent decrease in tissue oxygen delivery.[51]

Monitoring of ventilation

It is inconceivable today to ventilate a neonate without having access to real-time pulmonary monitoring. Almost all ventilators available in the anaesthesia setting display some waveforms, and it is vital that these should meet the criteria of a protective open-lung ventilation strategy. The classical pulmonary waveforms are represented by pressure, volume and flow displayed versus time. While the pressure and flow curves are specific for the ventilation mode used, it is crucial to focus on the flow versus time curve, which allows detection of the following features: (i) an interruption in the inspiratory waveform indicating a lack of time for equilibrium to be reached between the alveolar and the airway pressure, with the risk of inadequate lung inflation, and (ii) an incomplete deflation of the lung with the risk of auto-PEEP with overdistension of the lung and an enhanced risk of barotrauma. Thus, as regards the flow curve, it is essential to adjust both T_i and T_e, (either by changing the ratio or by decreasing the respiratory rate) to let the waveform reach the zero flow state before the transition to the next insufflation or exsufflation.[52]

The pressure–volume and the flow–volume loops afford an insight into the lung mechanics. The flow–volume loop is very useful for the detection of any change in the inspiratory or expiratory resistances. For instance, increases in airway resistance will be obvious in the flow–volume curve, with a concave expiration loop. The pressure–volume loop provides information on the dynamic

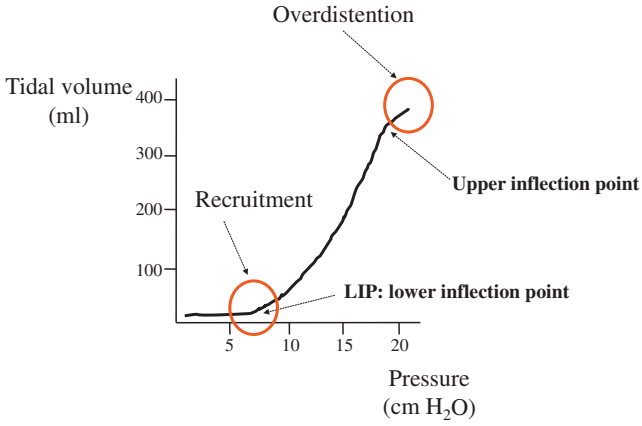

Fig. 1. Information provided by the pressure-volume loop.

compliance of the lung (defined by the slope of the loop), and also on the tidal volume, and facilitates establishment of the best PEEP level. Two inflection points characterise the loop. The first is at the lower part of the loop and corresponds to the beginning of alveolar recruitment. The lower flatter part can help in optimisation of the PEEP level, while the upper inflection point may occur at the end of the inspiration limb in cases of lung overinflation. In this situation, it is important to adjust V_t or the PIP to avoid any flattening of the upper end (Fig. 1).

Ventilation in transport

Transferring sick and unstable neonates between the ICU setting to the operating theatre is very hazardous. Transfer involves a higher risk of extubation, hypothermia, equipment and monitoring disconnection and also a risk of interruption to ideal ventilation modes and/or vital treatments such as nitric oxide. For sick neonates there should be a multidisciplinary discussion to decide whether the surgery can adequately be done in the ICU to prevent risk of transfer. This concept of surgery in the neonatal unit is no longer a novel one, for many studies have highlighted the beneficial effect of such practice on neonatal morbidity and mortality.[53] There are still some controversies surrounding the kind of procedures that can be performed in the ICU but a recent survey in the UK demonstrated that surgeons are becoming increasingly comfortable with performing laparotomy in very sick infants with necrotising enterocolitis in the ICU.[54] While the mortality following surgery for necrotising enterocolitis is more closely related to the severity of illness than to the location of the laparotomy, the transport of neonates weighing less than 1500 g to the operating theatre for laparotomy has been demonstrated to be associated with significant deterioration in a number of physiological parameters including oxygenation, which, in theory, may well impact on morbidity.[55] Thus, avoidance of the transfer of neonates weighing less than 1500 g in an unstable condition is nowadays encouraged. Surgery in the neonatal ICU maintains a continuity of care, but does require a surgical, neonatal and anaesthesia team that are comfortable with working together in that environment.

In other circumstances, transfer of a neonate with nasal CPAP is possible, especially as such devices are battery-powered. Regional anaesthesia for hernia repair for instance, can be performed while the child is under nasal CPAP, while more complex surgery may require that the trachea of the child be intubated with controlled ventilation.

Conclusion

The advances in technology over the last 20 years have led to the development of a variety of ventilation modes with confusing terminology, but which have undoubtedly contributed to the

advances in neonatal ventilation. It is important to note, however, that there is still no clear evidence as to the superiority of one ventilation mode over another with regard to the neonatal pulmonary and neural outcome. When applying the different available devices based on the newborn and premature respiratory physiology, clinicians should bear in mind that ventilation with a 'protective' and 'open-lung' strategy is essential to reduce the prevalence of bronchopulmonary dysplasia.

Practice points

- Match the characteristics of the ventilation with the pathophysiology of the patient.
- The choice of the ventilation mode should meet the criteria of protective open-lung ventilation strategy: 'Open the lung and keep it open'.
- Allow permissive mild hypercapnia.
- Real-time pulmonary monitoring should always guide the ventilation parameters.

Research agenda

- There is still a need for large studies to define the relevance of various ventilation modes;
- Utility of modern ventilation modes (such as the NAVA) in neonates;
- Establish evidence for the use of HFO ventilation and the reduction in the incidence of chronic lung diseases; and
- Better define the indications for non-invasive ventilation in the presence of respiratory distress syndrome.

Conflict of interest statement

None.

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