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D-16666-2009

Non-invasive respiratory support for neonates

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Foreword

Neonatal intensive care continues to be one of the most challenging fields in medicine. Fortunately years of experience from careful clinical observation, meticulous research and plenty of tender loving care have helped to significantly increase the chances of survival for our tiny patients. Of course, technological advances have also played a significant role. From the first newborn incubators, developed in the mid- and late 1800's and the first use of mechanical ventilation on a neonate in 1959 to the modern day ventilation devices, the science and the art of caring for premature infants has indeed come a long way.

This booklet is an attempt to address the current development process of non-invasive ventilation therapies, both from a theoretical and a practical standpoint. It is a matter of course that a work of this scope cannot cover all aspects of this complex field. Instead, our intention is to provide a review of the current understanding of the need for and the provision of respiratory support for neonates and to facilitate the application of these concepts to clinical practice. It is our hope that we can help provide a measure of objectivity in the complex decision-taking processes involved in the treatment of these most fragile of patients.

"Experience is perception that has been understood."
Immanuel Kant

Oxford, August 2017
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1. Introduction

The premature newborn and its specific challenges

1.1 Epidemiology of the premature newborn infant

The average duration of human gestation is 280 days. Prematurity is defined as birth before 259 days of gestation, or the 37th week of pregnancy. Each year, nearly 15 million babies are born prematurely[30]. Preterm birth rates vary significantly between countries: In the USA, 12–13% of infants are born prematurely, whereas in most European and other industrialised countries, preterm birth rates range between 5–9%[41]. Preterm birth accounts for 75% of perinatal mortality and more than half of long-term morbidity of all births[53]. Despite significant improvements in the management of preterm infants, complications of preterm birth continue to account for more than 15% of deaths in children younger than 5 years[41,62].

1.2. Specific challenges of preterm infants

Premature infants differ significantly from term born infants with regard to their physiology and pathophysiology. The pathophysiology of preterm infants also varies as a function of their level of immaturity. In addition, the inverse correlation between gestational age (GA) and disease severity has clearly been recognised[17]. Two particular groups of preterm infants are especially challenging for neonatal care teams: The very low birth weight infants (VLBWI, defined as birth weight < 1500g) and the extremely low gestational age infants (ELGANs, GA <28 weeks). Intact survival of the VLBWI and ELGAN depends on multiple factors. These vary according to the degree of antenatal care, time and place of birth and, consequentially, the local expertise and the equipment available to support the preterm newborn[3,35,55]. Since the VLBWI and the ELGAN suffer most from respiratory and gastrointestinal complications as well as from neurodevelopmental impairment, it is this patient group in which technological and medical advances will generate the most noticeable improvements[17,76].

1.2.1. Airway and breathing

The fetal development of the respiratory system is not concluded until shortly before the end of pregnancy,. i.e. term. Compared to term born infants, the preterm infant's chest is softer; this is largely due to incompletely ossified, cartilaginous bony structures. Even under normal atmospheric pressure, the trachea and larger airways are prone to collapse. The immature lung parenchyma contains fewer numbers of less developed gas exchange units. On the cellular level, type 2 pneumatocytes produce less surfactant, resulting in the reduction of pulmonary compliance when compared with termborn infants[15]. Further, the preterm infant's response to hypoxia

and hypercarbia is different to that of their term born counterparts, as they exhibit a noticeably irregular breathing pattern. This situation, compounded by decreased respiratory drive, can result in prolonged periods of apnea[64]. This combination of effects presents a significant challenge to successful pulmonary fluid clearance and alveolar aeration, thereby contributing to on-going respiratory compromise in preterm infants[33].

1.2.2. Feeding and growth

The preterm infant has reduced glycogen stores at birth and is at risk for hypoglycaemia, necessitating almost immediate nutrition[53]. Despite significant intestinal immaturity, solid evidence suggests that enteral feeding should be commenced within the first hours of life. Human breast milk should be used as soon as available. However, the optimal feeding volume and increment intervals have yet to be established[20]. To ensure adequate substrate intake, intravenous parenteral nutrition will be necessary for many preterm infants during the first days of life.

1.2.3. Immunity and infection

The VLBW and ELBW preterm infants are highly susceptible to bacterial infections. The use of endotracheal ventilation tubes places them at risk for ventilator associated infections. Indwelling catheters and extensive skin lesions from repeated blood sampling and instrumentation further increase the risk of hospital-acquired infections. Antibiotic treatment is a mainstay of neonatal care; nevertheless, specific pathogen selection through antibiotic treatment place preterm infants at risk for specific infections, such as necrotising enterocolitis. Hence, judicious use of antibiotic treatment is mandatory and good antibiotic stewardship has become the widely accepted doctrine.

1.2.4. Neuro-muscular and cognitive development

The disruptive environment of neonatal intensive care units (NICUs) per se can result in poorer growth and impaired neurosensory development[17]. Compared to term-born infants, preterm infants are more likely to show poorer overall academic achievement, exhibiting specific challenges in mathematical abilities and social relationships, as well as impaired emotional and physical development[76]. In general, the rate of developmental delay increases as a function of decreasing gestational age[17]. Bassler and co-workers used severity of illness as a predictor of neonatal outcome and established that a count of three neonatal morbidities bronchopulmonary dysplasia (BPD), brain injury, and severe retinopathy of prematurity is a strong predictor for the risk of death or severe neurosensory impairment, particularly in ELGANs[4].

2. Non-invasive respiratory support for neonates

2.1. Perinatal transition: from breathing liquid to breathing air

The fetus breathes: In utero, pulmonary epithelial cells secrete fluid which the fetus moves with breath-like motions from the lungs to the amniotic cavity. The presence of intrapulmonary fluid is an essential physiologic stimulus for normal fetal lung development and breathing movements are essential for conditioning the pulmonary tissue and the respiratory musculature for their functions after birth[33,66,82].

2.1.1. Pulmonary aeration - The significance of establishing functional residual capacity and tidal volume at birth

Once born, the infant must rapidly clear its airways. Pulmonary expansion is achieved by generating sub-atmospheric inspiratory pressures during the first strong diaphragmatic contractions[82]. The amount of air moved in and out of the lungs defines the tidal volume (Vt). With each new breath, more air enters the lungs than exits them, thus creating the functional residual capacity (FRC), which describes the amount of air remaining in the lung at the end of passive expiration[80]. A steady Vt and an adequate FRC are mandatory for efficient gas exchange because oxygenation is proportional to the patent alveolar surface area[66,68]. Hooper and co-workers recently proposed three distinct phases of initial lung aeration: The first phase involves alveolar fluid clearance into the interstitium, phase two marks a period of increased interstitial pressure due to the increased fluid load from intra-luminal fluid absorption, and phase three where alveoli and interstitial structures are ultimately sufficiently cleared for gas exchange[34]. Failure to clear the lung results in a functional reduction of alveolar surface area, insufficient gas exchange, and respiratory distress[40].

2.1.2. The origins of respiratory distress at birth

The preterm infant's respiratory system differs in many ways from that of the term infant; the chest wall and larger airways are cartilaginous, providing less resistance to atmospheric pressure. The pulmonary architecture and its biochemical properties remain at the very immature, saccular developmental stage where the surfactant system is not fully functional and luminal sodium channels are underexpressed[22,81]. The respiratory drive is poorly controlled by the immature respiratory centre, which is less sensitive to carbon dioxide and provides a less coordinated respiratory pattern[16]. These factors predispose preterm infants to insufficient generation of Vt and FRC. Thus, premature birth is associated with an increased risk of respiratory distress[79].

2.2. A history of non-invasive respiratory support of the preterm infant

The successes of neonatal medicine are very closely linked to advances in respiratory stabilisation and ventilation. In earlier ages of neonatology, the ability to ventilate a preterm infant marked the turning point for the survival of increasingly immature preterm infants. Exogenous surfactant replacement therapy further improved survival of preterm infants. Over the past decade, significant advances in the understanding of pulmonary aeration, respiratory drive and non-invasive respiratory management of preterm infants (including less invasive methods of surfactant replacement) have helped to further reduce morbidity in even extremely preterm and very low birth weight infants.

2.3. Respiratory support of the preterm infant

2.3.1. Mechanical ventilation and the onset of bronchopulmonary dysplasia

The introduction of mechanical ventilation (MV) to neonatal care in the 1960s hallmarked the beginning of improved survival in babies with respiratory distress. However, due to technological limitations of the early neonatal ventilators with regard to tidal volume delivery, MV was associated with many challenges. Not long after MV became available for use in preterm care, Northway and co-workers described a debilitating disease distinct to ventilated newborns, characterised by prolonged respiratory distress, oxygen dependency and reduced exercise tolerance. Due to the characteristic histopathological changes of the lung which included remnants of fibrinous exudate and scarring of the lung tissue, Northway coined the term “bronchopulmonary dysplasia” (BPD)[59]. Despite these findings, the discovery of the pulmonary compliance enhancing properties of exogenous surfactant replacement therapy in the 1990s meant that the primary focus of neonatologists remained on the refinement of MV for premature babies and newborns with compromised respiratory function. However, irrespective of many significant medical and technical advances in the care of preterm infant lungs and in keeping with,the concept of “alveolar arrest” in the aetiology of BPD, MV remains a significant contributing factor for BPD, due to the inflicted volutrauma, barotrauma, atelectotrauma and biotrauma on the developing lungs[37].

2.3.2. Pioneers of nasal continuous positive airway pressure

To help avoid mechanical ventilation in infants with respiratory distress, Gregory and co-workers introduced the concept of continuous positive airway pressure (CPAP) in 1971[31]. In their seminal papers on the use of CPAP in preterm neonates, Gregory et al. documented an increase in arterial oxygen tension in infants treated with CPAP: Whilst Gregory applied CPAP levels well above those used in later years (12 cmH_20), he found a significant reduction in mortality from infant respiratory distress syndrome[31,32]. Hence, the new treatment was understandably welcomed with great enthusiasm and hailed as the 'missing link' between pure oxygen administration and MV[39]. Indications for CPAP use in the pre-surfactant era were to support pulmonary aeration and prevent alveolar collapse to counteract the vicious cycle of pathophysiological events leading to respiratory distress syndrome, characterised by hypoxia, dyspnoea, atelectasis, hyaline membrane formation, and respiratory collapse. Nasal CPAP proved a viable option to avoid intubation and prevented the unwanted effects of MV on the preterm lung, i.e. reduced mucociliary clearance and risk of mucosal injury, pneumonia by minimising barotrauma and volutrauma of the airways and parenchyma, thereby preserving surfactant function[58].

Originally, CPAP was administered via a head box (the Gregory Box) and soon after via truncated endotracheal tubes[18,24]. However, the latter necessitated a cautious approach because of the inherent risk of complications, including nasal lesions or tube blockage from copious secretions. Hence, less invasive methods for CPAP delivery were sought and bi-nasal CPAP prongs subsequently came into use[49]. Since then, a multitude of nasal CPAP applications have been introduced, trialled and tested. Currently, evidence from meta-analyses of randomised controlled trials comparing different nasal interfaces for preterm infants with prolonged respiratory support points towards the superiority of short, bi-nasal prongs to apply CPAP to premature infants[14].

Further, the recently introduced small nasal masks as patient interfaces were generally positively received[21,36,38]. By the mid 1980's, the advent of more sophisticated modes of ventilation, more refined technology for MV and the success of exogenous surfactant replacement therapy in lowering the initial ventilation pressures and oxygen concentrations almost marked the end of the CPAP era. However, an early comparison of several North-American neonatal care centres with regard to the incidence of BPD described that the lowest rate for BPD was observed in a single centre which, to this day, avoids MV for neonates: The Presbyterian Medical Centre, Columbia University in N.Y, USA[1]. Despite this striking result, intubation and MV remained the standard of treatment for RDS for almost another two decades, until the use of CPAP was studied in larger randomised controlled trials[19,25,56,75]. These studies have helped change the paradigm from an invasive to a non-invasive approach in the treatment of RDS, even in very immature preterm infants[12].

2.4. Modes of non-invasive respiratory support

2.4.1. Continuous positive airway pressure

Since the first description of the Gregory Box, the components of CPAP-Systems have followed a common principle: Devices for CPAP-therapy include a patient interface (nowadays usually nasal prongs or masks), a set of pipes for positive airway pressure delivery, a heater and humidifier system and a CPAP-generator. The traditional waterlock CPAP-generator, commonly referred to as "Bubble CPAP", has become the mainstay of CPAP therapy over the past decade[50,57]. More recent developments include variable flow CPAP and biphasic CPAP (Bi-Level-CPAP or Si-PAP)[54]. Both modes aim to support spontaneous respiration through a reduction of the infant's work of breathing.

2.4.1.1. Traditional "water-lock" – or "Bubble-CPAP"

In their initial description of a neonatal CPAP device, Gregory et al. used a water-lock as CPAP-generator. Using a constant gas flow to the patient and immersing the expiratory hose of his head-box device in a basin of sterile water, the authors could vary the expiratory resistance and thereby the level of continuously applied distending pressure[31]. Several modifications of the Gregory principle have led to the widespread use Bubble-CPAP in many NICUs. However, according to a questionnaire study of German NICUs, the predominant form of CPAP is respirator generated, constant flow CPAP via the Dräger Babylog 8000 system[72].

2.4.1.2. CPAP-devices with variable gas flow

Variable-flow CPAP is based on the "Beneviste-principle". Here, a special nasal interface is required which utilises a fluidic-flip mechanism, the so-called Coanda-effect, to guide the direction of gas flow during in- and expiration. The Beneviste-principle is thought to reduce the infant's work of breathing[39]. Several commercially available, standalone CPAP-devices use this principle to provide variable flow CPAP. Further, several modern neonatal ventilators offer variable flow CPAP as a non-invasive support option.

2.4.1.3. Comparison of constant-flow CPAP with variable-flow CPAP

The physiological effects of different forms of CPAP have been investigated in in-vitro and in-vivo studies and arguments for and against the various CPAP modalities have been formulated[50] (Table 1). For bubble-CPAP systems, Lee et al. and Pillow et al. attribute the positive effects on the work of breathing to the "oscillating gas-column" in the expiratory limb[48,63]. Lee et al. were able to show that infants on bubble-CPAP systems, compared to constant flow, respirator generated systems, had

statistically lower minute volumes[48]. Pillow and colleagues found in sophisticated animal experiments that bubble-CPAP, as opposed to constant flow CPAP, reduced the work of breathing, improved gas exchange and increased lung volume[63]. Several authors, including Courtney et al., have reported a positive effect of Bubble-CPAP on oxygenation, which appears to be superior to that achieved using variable-flow. However, the statistically significant, positive effect on the work of breathing of using Bubble-CPAP as found in-vitro and tightly controlled animal experiments has yet to be replicated in clinical studies.

ADVANTAGES	DISADVANTAGES
Increases functional residual capacity	Increases risk of air leakage syndromes
Improves pulmonary compliance and reduces the work of breathing	High CPAP can lead to lung over-inflation, decreased compliance, and increased work of breathing
Splints airway and diaphragm	
Prevents alveolar collapse	Increased intra-thoracic pressure may reduce venous return to the right heart and reduce cardiac output
Reduces the alveolar-arterial oxygen pressure gradient	
Reduces intrapulmonary shunting	Lung over-inflation decreases tidal volume and may increase PCO_2 and the dead-space fraction
Reduces obstructive and mixed apnea	Air may escape into the stomach, causing gaseous distension (CPAP belly syndrome)
Conserves surfactant	After about 10 days of nCPAP, more than 10% of infants develop nasal complications (columellar necrosis, ulceration of the nasal cavity, or vestibular stenosis)
	Skin excoriation and nasal damage may give rise to bacterial infection, in particular by coagulase-negative staphylococci

Table 1: Advantages and disadvantages of CPAP therapy (modified from Mahmoud 2011)[50]

2.4.1.4. Early use of nasal CPAP – CPAP from birth

Using video documentation in the delivery room, O'Donnell et al. showed that approx. 80% of ELGANs do indeed show signs of breathing at birth[60]. Routine intubation of such infants will interfere with their physiological fetal-neonatal transition. Several large-scale clinical trials have compared the use of invasive to non-invasive respiratory support of breathing VLBWI and ELGANs from birth. Meta-analyses of these studies have shown significant positive impact on survival and overall pulmonary outcomes with no added negative effects in the non-pulmonary outcomes in the non-invasively managed patients[27,77]. The number needed to treat to save a VLBWI from death or BPD was between 25 and 35, respectively (Fig. 1). Follow-up stud-

ies of VLBWI treated with CPAP from birth compared to those who were routinely intubated and ventilated showed that pulmonary function was significantly improved at term equivalent age (higher respiratory compliance, lower elastic work of breathing and consequently improved respiratory rate and minute ventilation) (Figure 2)[73]. Consequently, the American Academy of Pediatrics has recently advised that preterm infants should be initially managed with CPAP, rather than intubation and ventilation[67].

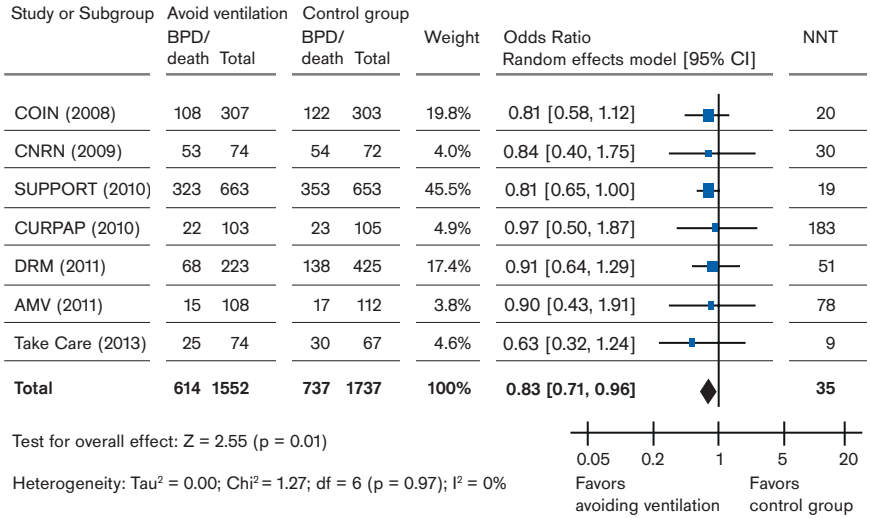

Figure 1. from Fischer H et al27. Pediatrics 2013; 132: e1351-60

2.4.2. Non-invasive intermittent positive airway pressure

2.4.2.1. A rationale for exploring alternative modes of non-invasive respiratory support

Studies of early CPAP use in VLBWI found that while a significant proportion of the <29 GA infants can be stabilised with CPAP[27,56,77], a fraction of these infants may require a brief period of mechanical ventilation, often limited to the first 72 hours of life[11,28]. However, once intubated, the incidence of successful timely extubation of VLBWI infants may be as low as 33%. Many of these infants require re-intubation due to their irregular respiratory pattern, resulting in prolonged apnoeic episodes and, consequently, profound desaturations. Therefore, instead of extubating VLBWI with the subsequent use of conventional CPAP, various alternative modes of non-invasive respiratory support have been studied[2,9,12,47].

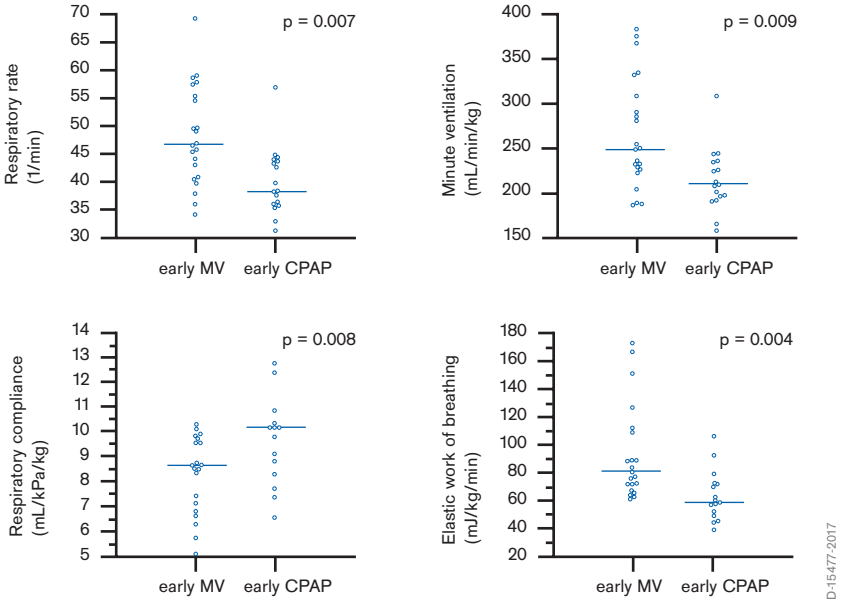

Figure 2: Pulmonary function at term equivalent age in VLBWI treated with CPAP (early CPAP) or mechanical ventilation (early MV) at birth. (Figure by G. Schmalisch, Berlin, taken from data as in Roehr CC et al. ADC F&N Ed. 2011)[73]

2.4.2.2. A definition of non-invasive intermittent positive pressure ventilation

Non-invasive positive pressure ventilation (NIPPV) describes the nasal or pharyngeal application of intermittent peak inspiratory pressure (PIP) inflations on top of CPAP. A recently introduced variation of this includes the use of nasal/pharyngeal high-frequency oscillation ventilation. The general assumption is that the PIP applied to the nasopharynx travels down the distal airways and into the gas exchange units, similarly to invasive mechanical ventilation. This is thought to result in an elevated mean alveolar distending pressure, which augments tidal volume and supports spontaneous breathing while protecting the airways from alveolar collapse during apnea[12,69]. However, the precise mechanisms of action, the benefits and limitations of different currently available devices and offered modalities, as well as the choice of applicable settings have not yet been fully explored[5].

2.4.2.3. Clinical applications of non-invasive intermittent positive pressure ventilation

Indications for using neonatal NIPPV include situations in which primary and secondary respiratory support may be required. This is chiefly either as a preventative

measure, i.e. to avoid endotracheal intubation and ventilation, or following extubation. In both scenarios, NIPPV would be used either to bridge apnoeic episodes or for severe apnea-bradicardia-syndrome[2]. In practice, an invasive ventilation mode is chosen on the ventilator (IMV, HFOV, etc.) or special commercial devices (Bi-PAP or Si-PAP modes) and intermittent positive airway pressure (IPPV) is applied via the non-invasive patient interface (nasal prong or mask)[23].

2.4.2.4. Non-synchronised and synchronised forms of non-invasive intermittent positive pressure ventilation

At present, there is a paucity of data for recommending the optimal PIP level, optimal delta between PIP and PEEP, inspiratory time or respiratory rate5. Studies differ regarding the level of applied PEEP (5-8 cmH_2O) and PIP (10-20 cmH_2O), the delta P between pressures (0 to 3cmH_20), inspiratory time (0.3 - 1s) and backup rate[42,45,46,54,61]. Therefore, Clauret and Bancalari recently concluded that non-synchronised NIPPV was no more effective in treating apnea, bradycardia or hypoxic episodes, nor does it seem to improve CO_2-removal more effectively than CPAP[5]. However, the latest generation of mechanical ventilators now offers synchronised forms of NIPPV, and first studies show promising results[23,29,58]. Therefore, the results from studies on the efficiency of synchronised NIPPV performed with comparable protocols and devices are eagerly awaited.

3. Future developments in non-invasive respiratory support of neonates

3.1.1. Nasal high-frequency oscillation ventilation

Following anecdotal reports on the use of nasally applied, high-frequency oscillation ventilation (nHFOV) in neonates, DeLuca and co-workers performed and in-vitro study to examine the effect of applied nHFOV amplitude and recorded tidal volume and found a quasi-linear relationship ($r2 = 0.99$)[13]. Other authors have reported individual cases or small case series on the clinical application of nHFOV, proving its feasibility and demonstrating adequate CO_2 elimination[6,10]. Recently, Fischer et al. surveyed 172 European NICUs with respect to their use of nHFOV and found that less than 20% of units use this form of non-invasive respiratory support26. Prospective clinical trials on nHFOV in neonates are currently under way.

3.1.2. High-flow nasal cannula therapy

Recently, the application of medical gases at high flow rates via small nasal cannulae has found its way into the respiratory management of neonates[43,50]. This

treatment form, in which tiny nasal cannulae are used to apply heated and humidified gas at flow rates between 3 and 8L/min, is commonly referred to as nasal high-flow therapy (nHFT) or high-flow nasal cannula therapy (HFNC). The cannulae used in nHFT are much smaller than conventional CPAP prongs or masks and, possibly for this reason, appear to be tolerated much better than conventional CPAP applications. Evidence from large clinical trial has helped to establish nHFT as a means to manage neonates post extubation[8,12,52,70,84]: There is currently not enough evidence to support their use as primary therapy for infants with RDS from birth[74].

3.2 Non-invasive respiratory support and developmental care aspects

Efforts to optimise developmental care of preterm infants focus on minimising handling, including parental engagement in care, reducing the number of painful procedures and finding the least invasive means of applying respiratory support[76,84]. Most forms of non-invasive ventilation appear favourable over the use of invasive means of ventilation when it comes to supporting the cognitive and motor development of preterm infants. Therefore, the least invasive treatments, such as nasal CPAP and nHFT may be less detrimental to normal neonatal neurological development. This becomes especially clear when one considers that their application requires less sedation than is usually required for ventilated infants. However, only a limited amount of research has addressed this specific question to date[46].

Research in developmental aspects of nasal CPAP and nHFT is underway. Koenig et al. and Roberts et al. recently investigated the extent of noise generated by nHFT compared to conventional CPAP[43,70]. The groups found conflicting results; while Koenig et al. found the nHFT to be exponentially louder than CPAP[43], Roberts and co-workers found no statistically significant difference between both modalities[70]. The developmental impact of this noise factor has not yet been prospectively assessed. As for the practical application of nHFT, Roberts et al. recently surveyed Australian NICU personnel with regards their preferences and perception of CPAP or nHFT in the care for preterm infants. The authors found that neonatal nurses preferred nasal CPAP for post-extubation support of infants <28 weeks' gestation and nHFT for infants of 28 or 30 weeks' gestation. Authors conclude that this provides evidence for nurses preferring nHFT over CPAP in preterm infants ≥28 weeks' gestation[70]. Although less systematically surveyed, parents seem equally in favour of nHFT for its simpler application and facilitation of parent involvement in the infant's care[71]. To summarise, while distinct differences between various forms and devices for neonatal NIV are clearly recognised, the potential developmental impact on the infant has not yet been sufficiently assessed and constitutes a fascinating topic of ongoing research[23,45, 74,85.]

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Moving from theory to practice can be challenging. The clinician's task is to translate such theoretical considerations and interpret the results of scientific experiment and clinical trials into meaningful bedside management options. The purpose of this booklet is therefore twofold. Firstly, it is intended to serve as a compendium of current knowledge on the subject of neonatal and paediatric ventilatory support. Secondly, it provides practical information and instruction on how to use that knowledge in a clinical setting with the help of the Dräger Babylog VN 500*.

In this section, you will discover how to set up the Babylog VN 500 as well as how to use its various ventilation modes. In addition, important differences between paediatric and neonatal patients are discussed. Naturally, it is beyond the scope of this text to dictate particular indications for ventilation therapy. This task will always remain in the hands of the clinician. Instead, it must be considered as a framework within which the clinician can take evidenced-based decisions and then apply that evidence to the practice of mechanical ventilation.

*Infinity Acute Care System Workstation Neonatal Care

Babylog VN 500 – Non-invasive ventilation

For neonatal and paediatric patients requiring ventilatory support, the last several decades have brought about a paradigm change characterised by a steady transition from mechanical ventilation to less invasive methods. The rationale for the use of non-invasive ventilation (NIV) includes the avoidance of the adverse effects of mechanical ventilation, such as VILI (Ventilator Induced Lung Injury) and BPD (Bronchopulmonary dysplasia). In addition, NIV opens up new treatment possibilities for conditions such as RDS (Respiratory Distress Syndrome) and facilitates early weaning strategies.
The Babylog VN 500 from Dräger is a dedicated neonatal and paediatric ventilator that provides tidal volumes up to 300 ml. The device is designed to cover the entire spectrum of modern therapy, from the ventilation of intubated patients to non-invasive ventilation and O_2-therapy. This chapter describes the use of non-invasive ventilation features of the Babylog VN 500.

Technical principle

Non-invasive ventilation can be catagorised in three different modes with various interfaces:

- constant pressure mode e.g. CPAP
- bi-level pressure mode e.g. PC-CMV
- O_2- therapy (which can be used for low- and high-flow oxygen therapy)

The following technical illustration applies only to non-invasive ventilation. The technical background of O_2-therapy is explained later in this chapter.
Modern ventilators use different flow principles to generate pressure in the hose system. The underlying technical principle that allows the Babylog VN 500 to provide the flow necessary for the therapy incorporates a constant base flow, also referred to as continuous flow, of 6L/min (neonates) and 3L/min (paediatrics) and an additive demand flow (see Figure 1). The constant base flow facilitates spontaneous breathing by the patient and enables comfortable triggering in paediatric patients. The demand flow alters the flow from the ventilator towards the patient, compensating for the changes in pressure.

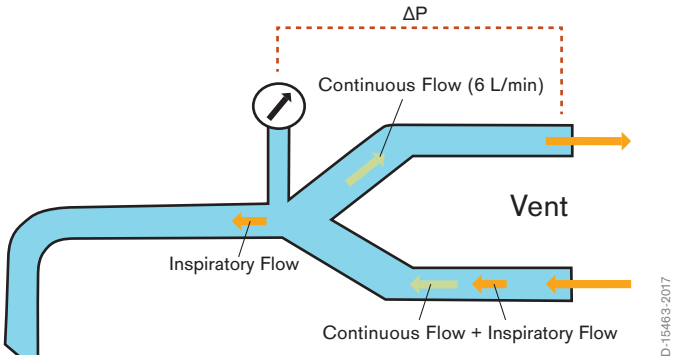

Figure 1: Flow principle of the Babylog VN 500

The Babylog VN 500 can regulate the flow in two ways. In the “system setup” menu, the user can select either the “inspiratory flow setting” (1) or the “slope setting” (2).

1) Operation with manually adjusted inspiratory flow

In this mode, the device functions much like a classic continuous flow ventilator. The inspiratory flow is set by the user to a constant litres/minute value. The inspiratory flow affects the speed from the lower to the upper pressure level and thus affects the applied tidal volume. During inspiration only, this set flow is delivered at maximum by the ventilator. If significant leakage in the patient circuit or at the prongs/mask is present or a high spontaneous flow demand from the patient is encountered, the total deliverable flow may be insufficient. As a consequence, the pressure in the circuit will drop. During expiration phase, the base flow is delivered. The inspiratory flow setting must be altered manually to adopt to a higher flower demand than set. The ventilator delivers only the flow that is required to stabilise the set pressure.

2) Operation with slope adjustment

This mode can be thought of as an automatic flow mode. The clinician sets the slope time, which is the time needed for the ventilator to build up the pressure to the set “Pinsp” level. Based on the slope time, the ventilator automatically adjusts the flow necessary to build up the pressure within the given time. The slope is adjustable in intervals of seconds. In addition to other factors, the amount of flow is dependent on the compliance and resistance of the hose system, the respiratory drive of the patient, lung mechanics and leaks at the patient interface. If significant leakage in the

patient circuit or at the prongs/mask is present or a high spontaneous flow demand from the patient is encountered, the device will automatically deliver more flow in order to compensate for the leakages and satisfy the spontaneous flow demand from the patient. Consequently, the pressure will be reached within the set slope time and will remain stable. When setting up this ventilation mode, the maximum allowed flow is initially set to 30L/min in neonates and 60L/min in paediatrics. The limit can be manually reduced if needed. However, the ventilator delivers only the flow needed to stabilise the selected pressure limit.

Slope and Inspiratory Flow Adjustment behave identically during the expiratory phase (in this respect, pure CPAP incorporates a continuous expiratory phase). During expiration, a base flow of 6L/min (in neonatal patient category) and 3L/min (in paediatric patient category) is delivered by the ventilator. If leakages in the hose system or mask and prongs are present, the ventilator will automatically provide more flow in order to compensate for the leaks and stabilise the pressure level. This additional demand flow is automatically delivered by the ventilator in order to stabilise the pressure level and reduce work of triggering and breathing (WOB).

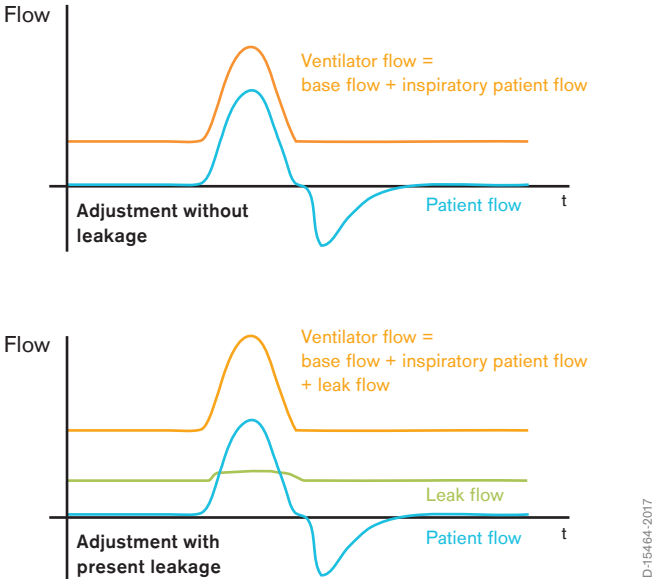

Figure 2: Flow adjustments with proximal flow sensor

Figure 2 illustrates the adjustment of the ventilator flow in the presence of leakage to stabilise the pressure when a proximal flow sensor is installed. The leak flow is determined by a model based on the discrepancy between inspiratory and expiratory volumes. It is added on the base flow and the measured patient flow. Changes in inspiratory flow or slope affect the inspiration phase. In slope mode, the ventilator flow is determined automatically. If the inspiratory flow is set manually, the maximum inspiratory ventilator flow will be limited to the set value.
If no proximal flow measurement (e.g. neonatal flowsensor) is installed no patient flow will be measured and base flow and leak flow only will be taken into consideration (see Figure 3).

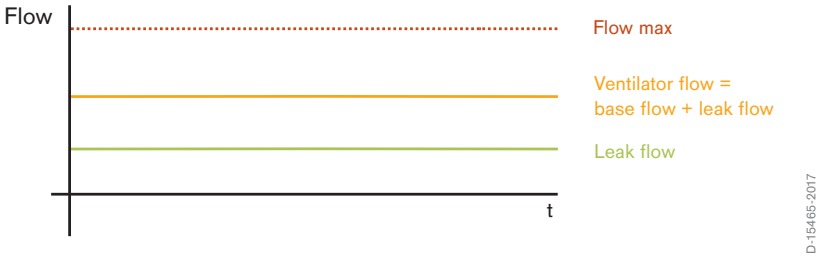

Figure 3: Flow adjustments without proximal sensor

Figure 4, 5 and 6 show screen shots from the Babylog VN 500 during different configurations. Figure 4 shows the CPAP mode with inspiratory flow adjusted to 5L/min. The CPAP pressure is kept constant.
Figure 5 and 6 illustrate a bi-level non-invasive ventilation with slope and inspiratory flow adjustment. The steepness of the pressure curve differs with the selected setting. According to Figure 5 the flow in the slope setting is regulated automatically to reach 18cmH_2O within 0.1s. Figure 6 displays the same settings with selected manual inspiratory flow. It shows that the flow is insufficient to built up the set pressure of 18cmH_2O. The fixed maximum inspiratory flow must be altered manually.

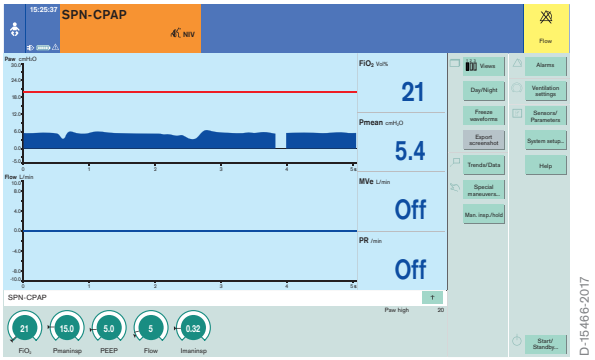

Figure 4: SPN-CPAP with manual inspiratory flow

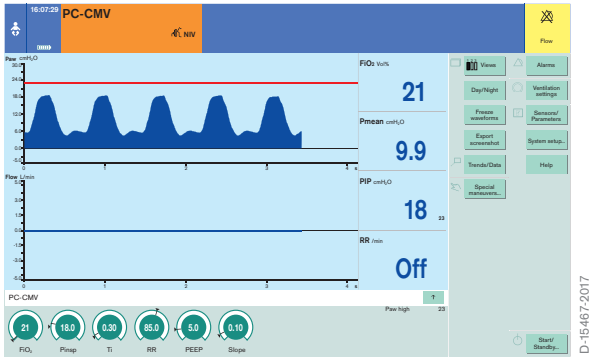

Figure 5: PC-CMV with slope adjustment

Figure 6: PC-CMV with manual inspiratory flow

Initiating non-invasive ventilation in the Babylog VN 500

Before beginning therapy, the non-invasive ventilation mode must be selected. The therapy mode can be easily changed from “Tube” to “NIV” at the Start-Standby dialog. Once selected, the NIV therapy mode is highlighted in orange.

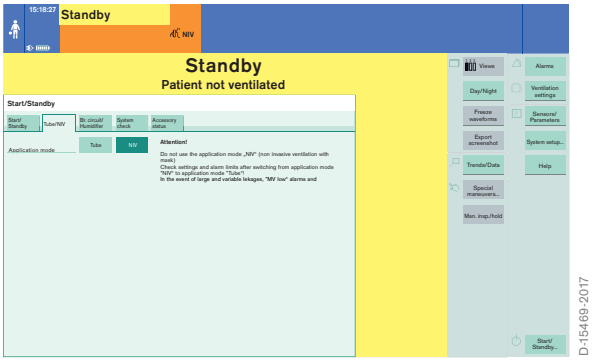

Figure 7: Set-up dialogue of NIV

Depending on the selected patient category, the functional capabilities of the Babylog VN 500 differ with respect to triggering and mode availability. For NIV, the following ventilation modes can be selected (see Figure 8).

VENTILATION MODE	PATIENT CATEGORY	
	PED. PAT	NEO.
PC-CMV	X	X
PC-AC	X	
PC-SIMV	X	
PC-PSV	X	
PC-MMV	X	
PC-APRV	X	
SPN-CPAP		X
SPN-CPAP/PS	X	
SPN-CPAP/VS	X	
SPN-PPS	X	

Figure 8: Ventilation modes

For this reason, paediatric and neonatal patients will be discussed separately in the following section.
Please note that High Frequency Oscillation is not approved for use in non-invasive ventilation. The Babylog VN 500 automatically switches to default modes when used for NIV:
– for paediatric settings to the SPN-CPAP/PS ventilation mode
– for neonatal settings to the SPN-CPAP ventilation mode.

Continuous positive airway pressure ventilation (SPN-CPAP)

Spontaneous breathing with continuous positive pressure level in NIV mode is available in both patient categories.
When spontaneous ventilation modes are employed, the patient provides most of respiratory work on his own. The PEEP level (CPAP) at which spontaneous breathing takes place can be adjusted.
The application of continuous positive pressure allows for a higher functional residual capacity (FRC), thus improved oxygenation and fewer collapsed alevoli. The improved pulmonary compliance leads to an increase in tidal volume and improved elimination of CO_2. The work of breathing can be reduced and events of obstructive apnea are less frequent.
Continuous monitoring of oxygen saturation, fixation of interfaces and sufficient humidification is required in order to guard against nasal complications and skin lesions. If indicated, suctioning should be performed regularly to prevent obstruction of interfaces.

Neonatal patients: Spontaneous Continuous Positive Airway Pressure (SPN-CPAP)

Spontaneous breathing with continuous positive pressure level in the NIV application mode.

This ventilation mode is only available for non-invasive ventilation in the neonatal patient category.
As explained in the section “Operation with slope adjustment”, the flow is either adjusted fully automatically or fixed at a maximum level depending on the configuration. As shown in Figure 6, in the presence of leak or high respiratory effort, a larger inspiratory flow may be required to maintain a stable pressure.

Figure 9: Neonatal patient in the mode SPN-CPAP

Prongs and small NIV masks are frequently used in neonates. For successful therapy, it is essential to heat and humidify the gas and to choose the correct interface size. Interfaces that are too small may cause excessive leaks, whereas excessively large interfaces may lead to fluctuating pressures. A proximal flow sensor cannot be installed in the neonatal patient category due to the added dead space.

Paediatric patients: Spontaneous Continuous Positive Airway Pressure (SPN-CPAP/PS or SPN-CPAP/VS)

In paediatric patients, the user can choose between spontaneous CPAP (SPN-CPAP) with pressure support (PS) or volume support (VS). To fine tune these settings to the patient's lung mechanics, the speed of the pressure increase for pressure and volume support can be defined using the slope or flow adjustment. As explained, both define the duration of the pressure increase from the lower to the higher pressure level. These settings directly affects the flow and thus the supplied tidal volume (VT).

In SPN-CPAP without PS, the patient breathes at PEEP level. If the patient is unable to manage the complete breathing cycle without assistance, additional pressure support can be activated. Every detected inspiration attempt at PEEP level triggers a mechanical breath. If the PS is set to zero, the patient will be ventilated with normal CPAP.

In SPN-CPAP with VS, the patient also breathes at PEEP level. In addition, the user can set a target volume (VT) so that the device generates the pressure necessary to apply the volume. If Pmax/Paw high auto-set is activated, the pressure will be limited by “Pmax” to meet the requirements under varying lung conditions. The Pmax/Paw high autoset describes the linking of the maximum pressure setting to the alarm limit airway pressure high (5mbar above Pmax). The patient’s inspiratory efforts are synchronised; in other words the time, number and duration of volume supported breaths are determined by the patient’s activity.
These modes are not available in neonatal patient category as a flow sensor cannot be installed during non-invasive ventilation.

Non-invasive Ventilation with Bi-level Pressures

For bi-level pressure support in the NIV mode, the two patient categories differ in terms of trigger options and availability of modes. While only one mode is available for neonatal patients, the clinician can choose from a wider range of ventilation therapies for paediatric patients.
Indications for this therapy option include avoidance of mechanical ventilation and support following extubation. It is used as a bridge across apnoeic periods and where primary or secondary respiratory support is required.

Neonatal patients: Pressure Controlled – Continuous Mandatory Ventilation (PC-CMV)

Non-invasive PC-CMV describes nasally or pharyngeally applied, intermittent peak inspiratory pressures (PIP) on top of CPAP pressure. Because it is an “open” system, it allows spontaneous breathing during the entire respiratory cycle. This mode is also known as NIPPV and, by adapting the settings, can be used as nBIPAP (Non-Invasive Biphasic Positive Airway Pressure).
The upper pressure level is determined by the inspiratory pressure (Pinsp) and the duration of the mandatory breaths is determined by inspiratory time (Ti). As in all pressure-controlled ventilation modes, the tidal volume supplied depends on the delta in pressure “Pinsp – PEEP”, the resistance and compliance of the patient’s lungs and the patient’s respiratory drive. Mandatory breaths are not triggered by the patient and inspiratory time is fixed to the set “Ti”. The number of mandatory breaths is set by the respiratory rate (RR). The pressure rise from the lower pressure level (PEEP) to the upper pressure level is determined by the slope or inspiratory flow

setting (see section “Operation with slope adjustment”). The ventilator can recognise disconnection and insufficient airway pressure without the help of a flow sensor. This mode is indicated for use in patients with apnea of prematurity, for initial treatment of RDS and for weaning of mechanical ventilation. The mandatory inflations reduce dead space ventilation and stabilise the functional residual capacity by elevating the mean alveolar distending pressure. In order to apply this ventilation mode, masks and prongs are used. The additional dead space must be taken into account and select interface must me correctly sized to prevent excessive leaks, obstruction and fluctuations in pressure levels.

Figure 10: Neonatal patient in the mode PC-CMV

Paediatric patients: Non-invasive ventilation with Bi-level Pressure

In contrast to neonatal patients, paediatric patients are not adversely affected by the additional dead space added to the system by the proximal flow sensor. Therefore, it is possible to select almost the same ventilation modes as in conventional ventilation (see Figure 4).

PC-CMV (also known as NIPPV) and PC-SIMV (also known as sNIPPV) are examples of possible options in non-invasive ventilation in paediatric patients.

With an installed proximal flow sensor, flow- and volume monitoring are available for functions such as Volume Guarantee and Mandatory Minute Ventilation (PC-MMV). If possible, it can be attached to the patient interface, e.g. NIV mask. With interfaces in which the proximal flow sensor cannot be installed, proximal flow monitoring must be switched off. If the flow sensor is deactivated or removed, the internal flow sensor on the inspiratory side of the device will be used for triggering. The base flow is

switched off and the device detects the pressure drop produced by the inspiration effort of the patient. The flow is altered and if the trigger criterion is met, an inflation will be initialized. The ventilator can recognise disconnection and insufficient airway pressure without the help of a flow sensor.
Interfaces such as masks, prongs and sometimes hoods are used.

O_2-therapy

High flow therapy (HFT) is a ventilation mode enjoying increasing popularity and acceptance in neonatal and paediatric patient populations. It is described as the application of blended oxygen at high flow rates through nasal cannulae. The medical gas is heated and humidified.
HFT creates a bridge between low-flow-oxygen therapy and CPAP.
The easy application and improved tolerance of patients and care givers have contributed to the increased usage of this form of therapy in recent years. It has the potential to reduce the need for intubation and CPAP through wash-out of dead space, improved mucociliary clearance and by creating a positive pressure in the pharynx[86].

Flow and oxygen concentrations can be set in the Babylog VN 500 when using the O_2-therapy mode.
The therapy option can be used for conventional oxygen therapy or high flow therapy to administer heated and humidified air.
In the Babylog VN 500, this therapy mode can be easily selected directly from the “Start-Standby dialog”.

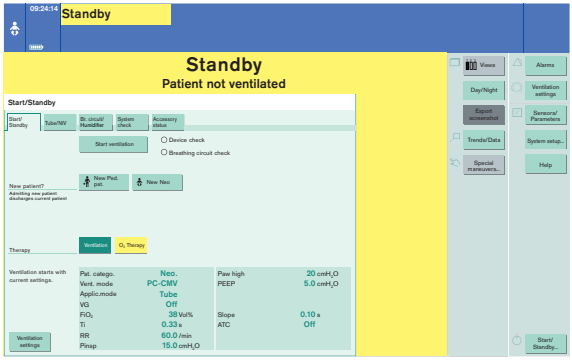

Figure 11: O_2-therapy dialogue

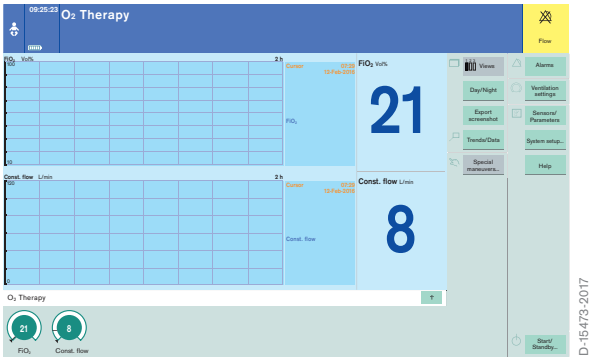

Figure 12: O_2-therapy

Compatible patient interfaces include nasal cannulae O_2-masks and hoods. NIV masks must not be used during this mode as these have no mandatory leak. Here, the patient would be jeopardised since the infant may not be able to exhale through the mask and the pressure is applied continuously. Flow, minute volume and apnea are not monitored in this mode. Hence, the use of external SpO_2 monitoring is recommended.

Usually, flow rates range from 2L/min to 8L/min for newborns and from 8L/min to more than 25L/min for paediatric patients. In the Babylog VN 500, it can be set from 2L/min up to 50L/min. The spontaneous peak flow is a good guide to estimate the amount of flow that is suitable for the patient. The setting should exceed the patient's peak flow in order to prevent inhalation of the entire delivered gas volume and to avoid dilution of the selected O_2-concentration with ambient air. The peak flow can be estimated by freezing the screen in a conventional ventilation mode. The cursor can then be used to toggle the maximum value. Usually, in Low birth weight infants, 3-4L/min of flow is sufficient. Unnecessarily high flows may result in high airway pressures.

The effectiveness of high flow therapy also depends on the selection of the correct prong size for the individual patient. It is important to maintain a leakage of approximately 50% at the nostril. In contrast to nasal CPAP, a leakage is required. It should be noted that manufacturers define a specific flow range for each prong size. If a high flow is applied to an interface with a small diameter and high resistance to

flow, the pressure will rise. As a consequence of exceeding the manufacturer's flow rate limits, the pressure in the patient circuit may rise above the set cut-off limit of 30cmH_2O and the system may stop the flow delivery and open the valve to the atmosphere.

Additional functions

Inspiration hold

The Babylog VN 500 offers a manual inspiration/hold manoeuvre in which the pressure of the breath is set with the "PmanInsp" therapy control and the duration of the breath is set with the "TmanInsp" therapy control. Two options are available to apply sustained inflation:

a) The manual inspiration can be applied between two mandatory breaths by pressing the start button and holding as long as deemed necessary. The pattern of the inspiration corresponds to the ventilation pattern of the current mode.
b) Regardless of the starting time, an automatic breath can be prolonged by the same manual operation.

A manual inspiration is triggered by briefly touching the button and an extended inspiration is applied by holding it. The Babylog VN 500 automatically terminates the breath after five seconds in neonatal patient category and after 40 seconds in paediatric patients.

The button can be found in the "Special manoeuvres" dialog or can be configured as a short link on the main screen.

Figure 13: Inspiration hold maneuver

Apnea ventilation in paediatric modes

The Babylog VN 500 can detect an apnea if the neonatal flow sensor is installed. This extended therapy mode for NIV ventilation is available only for paediatric patients.

If no expiratory flow is detected within a defined period of time (Tapn) Apnea Ventilation will be activated. If the patient stops breathing, Volume Guarantee ventilation at a set rate (RRapn), an I:E ratio of 1:2 and a set tidal volume (VTapn) will commence automatically. The Babylog VN500 ventilates in synchronised intermittent mandatory ventilation (PC-SIMV) mode. It can be reset via a button in the headline (Apn. Vent. reset), returning the settings to the prior ventilation mode.

In addition, the number of apnoeic events per minute can be analysed in a histogram in the trend dialog. The duration of the apnea is displayed in the alarm history and can be activated in the system setup. If the Automatic return from Apnea Ventilation function is configured, then the device will automatically switch to the previous ventilation mode when sufficient spontaneous breathing is resumed. Apnea ventilation must have been active for at least 2 minutes and the alarm message “MV low” is not active.

Apnea ventilation functions as back-up ventilation mode in spontaneous breathing modes to prevent desaturation and insufficient ventilation.

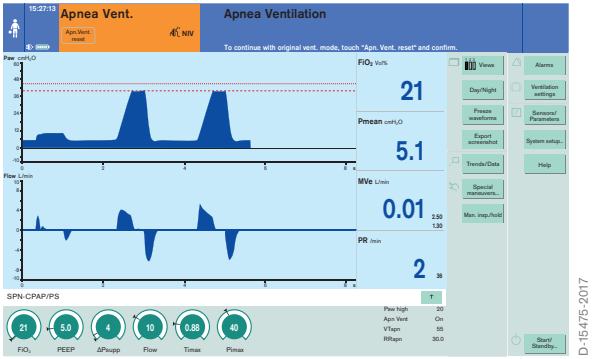

Figure 14: Apnea ventilation

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