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Noninvasive ventilation in children

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ABSTRACT: The use of noninvasive ventilation (NIV)/ventilatory assistance has in its modern form experienced a resurgence during the last two decades, primarily in the adult population.

During the last few years, NIV, predominantly in the form of positive-pressure ventilation/ventilatory assistance, has also become an option in the paediatric population. Although the technique is increasingly being applied, data in this often very heterogeneous group of patients are still very limited, and are usually derived from case series and not randomised controlled studies.

Available experience indicates that the technique is useful for children with a wide spectrum of hypercapnic and/or hypoxaemic respiratory disorders, in the acute as well as in the chronic setting. Results have shown improvements in survival and arterial blood gases, and have indicated better quality of life. Adverse effects are generally minor, although the impact on facial bony structures should be monitored closely during long-term ventilation.

Considering the paucity of data, the area badly needs research, which preferentially should include: 1) short- and long-term effects and adverse effects in various conditions and age groups; 2) techniques, in particular interfaces and triggering mechanisms; 3) comprehensive plans for training of attendants, discharge and follow-up; and 4) quality of life measurements. As many of the conditions suited for noninvasive ventilation are very rare, much of the research would probably benefit from multicentre studies, or even studies on a European level.
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During the last decade noninvasive ventilation (NIV) has been used increasingly to provide mechanical ventilation or ventilatory support to various groups of patients. Most of the experience originates from the adult population. Although an expanding area of interest, reports on the application of NIV in children have been scarce, and so far, case series constitute the vast majority of the available knowledge, both in the acute setting and in the home. Further, many of the published case series typically report the results from the treatment of a mixed group of children/conditions, making it even more difficult to draw conclusions with respect to any specific disease/condition. Recently, a consensus report summarised the present state of affairs as follows:

"At present, nasal mask ventilation in young children must be considered an investigational technique for research and/or use only by experienced centres. Further to our knowledge, there are no published reports on the use of this technique in small children, and there are no generally accepted guidelines" [1].

This review will report the available data for various groups of paediatric patients with respect to NIV in the acute and in the chronic setting, and underline the need for further research.

Presentation/symptoms

Although the basics of the respiratory physiology are similar in adults and children, major differences do exist, especially when comparing the very young child with the adult. The neonate is characterised by a relatively stiff lung and a very compliant chest wall

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that unopposed would lead to a functional residual capacity (FRC) of only 15% of total lung capacity. The actual value of 40% is maintained by a variety of manoeuvres including laryngeal breaking [2], maintenance of the post-inspiratory tone in the muscles of chest wall [3], and the use of respiratory rates fast enough to make the expiratory time less than the time constant of the respiratory system. The compliant chest wall impedes the neonate's ability to generate adequate tidal volumes (V_T) [4], increases the work of breathing (WOB) [5], by wasting force on chest wall distortion instead of generating effective alveolar ventilation [6], contributes to muscle fatigue [7] and accentuates growth retardation [8]. The mechanics of the respiratory system are further hampered by high-flow resistance of the nasal airway and small airways [9], increased propensity to hypertrophy of the adenoids and tonsils [10], a small zone of apposition of the diaphragm [6], horizontal ribs, and in the very young, immature muscles [11], all curtailing the endurance of the respiratory system. The metabolic rate is approximately double that of the adult, resulting in a ratio of alveolar ventilation:FRC of 5:1 in the infant compared with 1.5:1 in the adult [12], thus increasing the risk of hypoxaemia. Any parenchymal lung disease will increase this further. The hypoxaemic respiratory response is attenuated in the infant [13]. Apnoeas are more frequent than in the adult, they are more firmly associated to rapid eye movement sleep, which again is more abundant the younger the child is. During that specific sleep stage, muscle tone is particularly low contributing to a further decrease in FRC and in the power of the respiratory pump, while increasing the flow resistance of the airways.

Many children suffering from chronic respiratory insufficiency present predominantly with a hypercapnic profile based on hypoventilation rather than a hypoxaemic condition resulting from impaired pulmonary tissue function.

The hypoventilation disorders in children may, depending on the underlying condition, present in a variety of ways; ranging from insidious presentation during adolescence to infants being symptomatic from respiratory failure in the delivering room. Physical examination may reveal midfacial hypoplasia, an impaired nasal passage, enlarged tonsils, retrognathia, short neck, or in the infant/child with neuromuscular disease, a bell-shaped chest, kyphoscoliosis, tachypnoea, intercostal retractions or paradoxical breathing. Others may show little or no physical signs of respiratory failure. Nocturnal hypoventilation may be asymptomatic or may be associated with symptoms such as nocturnal arousals because of hypoxaemia or hypercarbia, awkward sleeping positions, night sweats, morning headaches, irritability and others. Table 1 summarises the symptoms associated with (nocturnal) hypoventilation.

Pulmonary function tests may suggest respiratory compromise, but the most conclusive way to assess nocturnal respiratory insufficiency is by polysomnography (PSG) [14–16]. Unfortunately this service is usually available only to a limited extent. A recent survey reported that only 2.5% of North American sleep laboratories responding to the questionnaire would perform PSG in children [17].

Table 1. – Symptoms associated with nocturnal hypoventilation

Nocturnal arousals
Awkward sleeping positions
Night sweats
Morning headaches
Daytime drowsiness or daytime hyperactivity
Behavioural and cognitive problems
Failure to thrive
Recurrent airway infections
Cor pulmonale (late manifestation)

Modalities

The rationale for respiratory support is in many, typically neuromuscular, conditions associated with carbon dioxide retention, to unload the respiratory muscles and to substitute the failing respiratory pump, in particular during sleep. NIV has thus in the adult population been shown to reduce the diaphragmatic electromyographic activity, the transdiaphragmatic pressure, the pressure-time index, and consequently to reduce WOB and the respiratory rate, and to increase V_T [18–21]. Supplemental oxygen in these conditions will not solve the problem, but may in fact make it worse. In the case of hypoxaemic respiratory failure, correction of shunt and ventilation/perfusion mismatch or associated apnoeas may be alleviated by ventilatory support and sometimes supplemental oxygen.

Noninvasive ventilation

NIV is based on the cyclical application of a positive pressure (or volume) to the airways. Previous studies have used volume-targeted ventilators [22, 23], but recently most studies have reported the use of positive pressure-targeted units. Using a pressure-targeted respiratory assist device, the ventilation achieved from a preset airway pressure (inspiratory positive airways pressure (IPAP)) varies with user effort and the mechanical characteristics of the respiratory system, such as compliance, resistance, auto-positive end-expiratory pressure, the ventilatory frequency and potential leakage. When applying respiratory assist, the trigger function, usually sensed as either pressure or flow changes in the system, is of fundamental importance. In the case of a small or weak child, inspiratory flows generated by the child may be insufficient to activate the trigger. This is further complicated by the volume added by the humidifier, which in children is often interposed. Not surprisingly, some authors have chosen protocols where the setting of the rate of the ventilator is slightly higher than the child's spontaneous rate, thus effectively instituting a controlled mode of ventilation [24]. The expiratory trigger often functions purely as a function of time, or as a function of a defined decline in inspiratory flow. In the case of (permanent) leaks,

inspiration by the machine may continue well beyond the point where the user has ceased to inspire, thus impeding expiration and adding to the WOB, to the discomfort of the child and the increased risk for gastric inflation. This may add a restrictive element to the respiratory system or even provoke aspiration. If supplemental oxygen is added, this is usually *via* the single hose system or *via* the mask. Accordingly the inspired oxygen fraction (F_{I,O_2}) will vary as the ventilatory pattern changes, although usually never above 0.5 due to the high-flow rates used in pressure-targeted ventilators.

Volume-targeted ventilators deliver a set flow to the users' airways for a timed interval and at a specified frequency, or in response to an inspiratory effort. This terminates when a preset volume has been delivered. When using a noninvasive mode, this technique is associated with leaks, and unless the machine is able to deliver a V_T up to twice the size of that needed for an intubated patient [25], can lead to diminished gas supply and discomfort for the ventilator user.

Negative-pressure ventilators repeatedly apply a subatmospheric external pressure to the trunk or just the thorax using a tank, a chest shell or a suit, thus imitating physiological negative-inspiratory pressure swings. Theoretically, this might be advantageous in children with right heart failures, as has been shown in the perioperative setting [26]. They are, however, often cumbersome and are associated with difficulty in performing personal care, with skin injury and with obstructive apnoeas that can be eliminated by positive-airway pressure (but not by supplemental oxygen) [27, 28]. In addition, they are often not equipped with monitoring devices. The use of negative-pressure ventilators is at present limited.

Interfaces

Comparative data on noninvasive interfaces in the paediatric population are virtually absent in spite of the crucial role this piece of equipment plays, both with respect to successful ventilation and to adverse effects. In addition, there is an appalling paucity of masks available for paediatric use. This area badly needs research and development. Contrary to adult studies, nasal masks seem to be the preferred type, both in the chronic and acute settings, even though children in the studies were often past the age of obligatory nose breathing. The interfaces have included standard masks, moulded masks and modified nasal cannulae, and in some cases full-face masks [24, 29]. The risk of aspiration, difficulty with regard to proper fitting of full-face masks in the chubby toddler, problems with cooperation and increased dead space might explain the frequent choice of nasal masks.

When using nasal masks, transparent models should be preferred to allow easy inspection of the nostrils to ensure that they are not partly or totally occluded from secretions or from dislocation of the mask. The risk is higher the smaller the child, since dimensions are smaller, and even a small displacement can result in interference with unobstructed delivery of positive pressure to the airways. Owing to the dynamics of the facial contours resulting from growth of the child, the proper fitting should be re-evaluated regularly. Masks should aim for the lowest skin pressure compatible with effective ventilation. Pressure marks should be looked for and, in particular, adverse effects on the maxillar bone, preferably monitored by serial lateral radiographs of the skull. In particular, attention should be paid to the risk of narrowing the bony airway in the anterior-posterior plane, in addition to the aesthetic risks. Change of mask position and/or mask shape and equipment for countertraction can be options to minimise damage. To the author's knowledge, no data on the reversibility of the adverse effects in this group of children is available. It is of interest to know that the growth potential, and thus potential reversibility of the damage, of the maxilla is less than that of the mandible. High priority should be given to aim for the smallest mask possible to minimise dead space and to facilitate trigger function. Elimination of carbon dioxide can be enhanced by adding an extra exhalation port in the mask. Oral leaks can be reduced using a pacifier, or in older children, a chin strap. Positioning of the child to allow for an unobstructed airway and for the free movement of the thorax and abdomen will also tend to reduce leaks. Tightening the mask straps, to minimise leak, to the extent that skin injury and cranial deformation occurs, should be avoided. Some leakage is acceptable, and the ventilators often used for noninvasive ventilatory support work well in the presence of leaks. In fact, some of them require a leak to function correctly [30]. The use of a full-face mask carries the risk that the mandible will be pushed backwards (not as a result of long-term use, but immediately after mounting the mask), and thus tend to obstruct the airway. Aspiration is also a concern [31].

Sometimes, custom-made masks are preferable, but in the opinion of the author, not always. Some of the moulded masks may be associated with a larger pressure drop probably due to small irregularities of the apertures followed by turbulent flow. It is therefore recommended always to check the pressure drop across the mask before clinical use. Appropriate headgear should be a concern, and in small children custom-made versions are often preferable. The material should be soft and allow for sweating and at the same time secure so that the mask stays in place, yet not exert focal pressure on the skull with the risk of producing cranial deformity in the neonate. If supplemental oxygen is added, high-flow rates are usually necessary because of the high-background flow rate, although the problem can be reduced somewhat if the oxygen is bled into the port of a mask, preferably with minimal dead space.

Although the use of noninvasive positive-pressure ventilation has increased markedly in the paediatric population very recently, the vast majority of children (receiving long-term ventilation) are still ventilated *via* tracheostomy [32]. The technique usually secures effective ventilation, and allows suction, as well as manual ventilation with large V_Ts (to recruit secretions and atelectasis). Tracheostomy can interfere with

phonation, in particular, in very small children, and is often associated with secretions and lesions of the stoma and/or the tracheal wall. Swallowing can be impaired due to the volume of the tube and also because the tube may fix the larynx, and thus prevent its upward movement during the swallowing procedure, important in protecting the airway. There are no generally accepted guidelines for when ventilation *via* tracheostomy is indicated, and the question is still an issue of controversy, but many clinicians will choose this mode either when bulbar function is impaired to some extent, when the need for respiratory assistance exceeds a major part of the day or when noninvasive interfaces are not accepted.

Humidifiers

Dryness of the upper airways is a common complaint from users of NIV [33]. The unidirectional flow from noninvasive positive-pressure ventilation (NPPV) prevents the recovery by the nasal mucosa of one-third of the water delivered through the airflow, leading to an increase in the nasal resistance [34]. This could, in turn, once the child is no longer an obligatory nose breather, lead to mouth breathing and associated leaks, which in adults has been shown to increase nasal resistance by up to six times the baseline value [34]. Considering that the area of any tube is reduced by the radius of the fourth power, any retention of secretions in the small airways of an infant is likely to increase the WOB considerably, and should be avoided. Humidification is one of the means. Heated humidifiers are much more efficient than passover humidifiers. The addition of a humidifier will add to the resistance of the circuit, and will tend to interfere with triggering and possibly pressure delivery.

Selection criteria for noninvasive ventilation

There are no published and generally accepted criteria for NIV in children. A recent consensus conference [1] listed clinical and physiological criteria for respiratory insufficiency due to central nervous system, neuromuscular and skeletal conditions in infants. These are summarised in table 2.

Many clinicians would use a combination of symptoms and clinical signs, (sleep-related) carbon dioxide retention and/or hypoxaemia as a premise for offering NIV. Some would include pulmonary functions tests (where applicable) [35], arguing that respiratory failure is unlikely if vital capacity (VC) >20% and/or if respiratory muscle strength is >30% of predicted value, and others [36] that a peak flow <180 $L \cdot min^{-1}$ is not sufficient to clear secretions. Preventive NIV has not been proven effective [37].

Contraindications have not been defined. Severe craniofacial malformations, marked bulbar impairment, profuse secretions, inability to ventilate sufficiently, and child and/or parents inability to cooperate would seem to be possible contraindications [31]. Nonacceptance by parents or staff at the hospital clinic has been reported as a reason for terminating treatment [33] with continuous positive airways pressure (CPAP) in children with obstructive sleep apnoea.

Initiating noninvasive ventilation in children

There are practically no data emanating from studies of any kind on how to initiate NIV in children. The present body of knowledge is constituted by the experience of clinicians working in the field, and a variety of routines are applied. Before NIV is planned, a diagnosis and a well-defined baseline profile, preferably including a PSG investigation, should be in place.

Whenever possible at all, any ventilatory support/NIV should begin on an elective basis. This leaves room for information, and for the parents and/or the child (whenever they are capable) to make an informed choice, and subsequently to adjust to the new situation mentally and with respect to practical matters. Information and discussion of the options should take place well in advance, and short- and long-term consequences for the child and the family should be explained. The goal of an increased quality of life and often also a prolongation of life should be clear. Acquisition of funding should have a high priority very early in the process. The stay at the hospital/clinic should be well planned, and will usually last a few days (unless the case is a child ventilated *via* a tracheostomy; in this case ~3 weeks are often needed). When relevant and possible, a group of attendants should be hired and, usually together with the parents, at the centre for ventilatory support/home mechanical ventilation educated to care for the child and to handle the respiratory assistance. It is recommended that the education should be structured and documented according to a well-defined educational programme. It is important that the carers are individually trained to perform the tasks associated with the total care of the child. The role of the attendant should be clear, as should that persons area of responsibility. Training should include signs and symptoms indicating the need to seek advice or assistance. Before discharge the child's condition should be stable, the ventilation documented to be effective and satisfactory, and the family and attendants ready and motivated.

Table 2. – Criteria for respiratory insufficiency

Clinical criteria	Physiological criteria
Weak cough, retained airway secretions	Vital capacity <15 $mL \cdot kg^{-1}$
Increased use of accessory muscles	Inspiratory force <20 cmH_2O
Incompetent swallowing, weak or absent gag reflex, decreased level of normal activity/function	P_{a,CO_2} >6.0 kPa (45 mmHg) P_{a,O_2} <9.3 kPa (70 mmHg) S_{a,O_2} <97% on room air

P_{a,CO_2}: arterial carbon dioxide tension; P_{a,O_2}: arterial oxygen tension; S_{a,O_2}: arterial oxygen saturation.

The ventilator-dependent child

The child receiving NIV should still be perceived as that unique child, and not primarily as a ventilator user. The equipment should be an aid, not the area of focus from the surrounding world. Networking with other children with a similar condition can contribute to self-assurance and role identity. On the other hand, integration with children without any respiratory (or other physical) insufficiency is desirable as a mechanism of integration and social mastering. It is important that, to the extent the child is able to respond to, an attitude of self-directed living and an active life is encouraged. As the respiratory insufficiency is usually just one of several physical disabilities, it is necessary to establish a total management plan to make premises for a good quality of life as good as possible. This does require the coordinated work of several partners, such as parents, attendants, the centre for home mechanical ventilation, physiotherapists, social workers, teachers and sometimes ventilator users' associations.

Complications of noninvasive ventilation

Complications are summarised in table 3.

Monitoring

At discharge a plan for future monitoring and follow-up must be outlined. Monitoring could take place at different levels. A thorough training and education of the child (where possible), the parents and the attendants at the centre for respiratory assistance/home mechanical ventilation, constitutes an important basis for qualified monitoring of the clinical condition once the child is living at home. A hot line or other ways of easy access to the centre of competence will also increase the level of monitoring. Depending on the condition, follow-up could take place typically every 3–6 months with an overnight hospital stay. Generally the younger and/or the more unstable the child is, the shorter intervals should be between hospital visits. Apart from clinical evaluation and history investigations, pulmonary function tests and cardiopulmonary monitoring and/or polysomnography should be included [16]. It is valuable to record as part of the PSG, the mask pressure to monitor the delivered pressure, leaks and synchrony between the ventilator user and the ventilator. The evaluation could also include radiographs of the thorax and the skull (lateral projection), arterial or capillary blood gases, body weight and height. A measure of quality of life would be desirable, but the literature on that subject is unfortunately almost nonexistent. A suggestion for parameters to monitor in the course of the disease is presented in table 4.

Table 3. – Complications related to noninvasive ventilation in paediatric ventilator users

Nasal and pharyngeal dryness
Vasomotor rhinitis
Air leaks
Skin irritation on the nasal bridge
Gastric distension
Air flow-induced arousals
Possible increase in work of breathing in user machine dysynchrony/compromised triggering
Carbon dioxide retention associated with large dead space
Impaired growth of facial bony structures

Outcome

Noninvasive ventilation in the acute setting

There is a paucity of data regarding the effect of NIV in children in the acute setting. One of the largest studies is a retrospective study [38] including 28 children with a median age of 8 yrs (range 4–204 months), treated on a continuous basis in an intensive care unit (ICU) for acute hypoxaemic failure using a bilevel positive airway pressure (BiPAP) assist device in the spontaneous mode *via* a standard nasal mask. The most common primary diagnosis was pneumonia, and nine children suffered from underlying neurological disease. Excluded were children suffering from sleep apnoea, from hypoventilation associated with neuromuscular disease or who received NPPV outside the ICU. Median period of ventilation was 72 h. Within the first hour of ventilation with pressure settings of 12 and 6 cmH_2O for inspiration and expiration, respectively, and supplemental oxygen at the discretion of the attending physician, arterial carbon dioxide tension (P_{a,CO_2}) decreased from 6.0±1.5 to 5.2±1.1 kPa (45±11 to 39±8 mmHg; $p<0.01$), respiratory rate from 45±18 to 33±11 per minute and arterial oxygen tension (P_{a,O_2})/F_{I,O_2} increased from 141±54 to 280±146 ($p<0.001$). No adverse effects on the circulation were noted, and complications were generally minor including ulceration of the nasal bridge. In another group of children suffering from status asthmaticus treatment for 13.5 h with NIV using BiPAP with IPAP/expiratory positive airways pressure (EPAP) settings of 13±3/7±2 cmH_2O (mode not reported), resulted in avoidance of intubation in 19 of 26 children, and a significant ($p<0.05$) reduction in F_{I,O_2}, respiratory rate and cardiac frequency was noted. Several did not tolerate NIV due to agitation, abdominal distension or deteriorating respiratory status [39].

Recently, PADMAN *et al.* [40] presented prospectively collected data from a paediatric intensive care unit (PICU) comprising 34 critically ill children with

Table 4. – Parameters monitored for initial diagnosis and during follow-up hospitalisation in children treated with noninvasive ventilation

Clinical history, including developmental milestones
Clinical evaluation, including height and weight
Nocturnal respiratory monitoring, including S_{a,O_2} and carbon dioxide values (preferably PSG with mask pressure tracing)
Radiograph of chest and lateral projection of the skull
Possibly arterial or capillary blood gases
State of the mask

S_{a,O_2}: arterial oxygen saturation; PSG: polysomnography.

underlying medical conditions treated continuously with BiPAP in the S/T-mode for a median duration of 6 days using IPAP/EPAP settings of 7–12 and 3–5 cmH_2O, respectively. Diagnoses included pneumonia, asthma, postoperative hypoventilation and sleep-aggravated breathing disorders. Mean age was 11 yrs. After 72 h of ventilatory support P_{a,CO_2} was reduced from 8.4±0.5 to 6.1±0.4 kPa ($p<0.05$), bicarbonate concentrations from 30 to 24 mM ($p<0.01$), and respiratory rate from 39 to 25 breaths·min^{-1} ($p<0.04$). Three (8.8%) required intubation. The only complication reported was skin breakdown over the nasal bridge of four patients. The combined treatment with NIV and expiratory support (manual and assisted coughing) in the PICU was applied in a prospective case-control study in 10 children aged 12–20 yrs in acute respiratory failure and suffering primarily from neuromuscular disease. All had no ventilator-free time, and six were originally intubated. Most used BiPAP (mode not indicated) with IPAP/EPAP settings of 24 and 3 cmH_2O, respectively. The four patients who originally used NPPV continued in that mode successfully, and the six others were all extubated mostly to a mouthpiece or a nasal interface. The authors point out that patient cooperation was critical for success [41]. In spite of this, the same group [24] reported that NIV *via* a nasal mask was successful to a large extent in 11 very young children aged 6–26 months with severe skeletal and bulbar weakness due to spinal muscular atrophy (SMA) type 1. Initially the children were ventilated *via* an endotracheal tube. Insufflation/exufflation was delivered *via* the tube at inspiratory/expiratory pressures of 25–40/-24–40 cmH_2O, respectively. Following extubation the children were managed according to a well-defined protocol, including nasal ventilation for 10 of the children at IPAP/EPAP settings of typically >14/3 cmH_2O, respectively (one used a volume-cycled ventilator). This was supplemented with manual abdominal compressions during the exufflation phase of mechanical insufflation/exufflation. The latter was provided *via* an oral/nasal interface. Protocol management was superior to nonprotocol management, with respect to establishing functioning NIV ($p=0.001$). Following the acute scenario, two children required continuous noninvasive support, six used only nocturnal nasal ventilation, two were tracheostomised and one was lost at follow-up. The shortcomings of the study include the small number of patients, a lack of controls and that a selection bias cannot be excluded. A case series of four patients suffering from SMA type 1 nasal ventilation and gastrostomy feeding failed to prolong life in the way that this strategy does in less aggressive neurological conditions, though it was effective acutely [42]. Several smaller case series support the positive effects of NIV in children suffering from acute respiratory failure [43–45].

Negative pressure ventilation in the acute setting

Negative pressure ventilation has been found to be superior to the use of oxygen alone with regard to avoiding intubation [46], and has compared favourably to the use of nasal CPAP in that respect [47]. It was also associated with a significantly lower incidence of pneumothoraces and bronchopulmonary dysplasia than was the case for intermittent positive pressure ventilation [48]. In a more recent randomised controlled study, SAMUELS *et al.* [49], over a period of 4 yrs in 244 neonates compared negative pressure support of -4–-6 cmH_2O with standard therapy that included CPAP of 4 cmH_2O, and demonstrated that the need for intubation was slightly less in the group ventilated with negative pressure devices, compared with the group that received standard therapy (86% *versus* 91%). Negative pressure ventilation using a chest cuirass was reported to be successful in a case series of critically ill children aged 4–16 months. Applied pressures were -18–-30 cmH_2O in conjunction with a CPAP of 6–10 cmH_2O [50].

Noninvasive ventilation in the chronic setting

Long-term use of NIV outside the hospital has in general increased markedly during the last few years, fuelled by improved technology such as simplicity of operation, portability, reduced noise and optimised algorithms. This is also to some extent true for the paediatric population, although full blown growth is still hampered by a lack of appropriate masks, among other things. In many places, NIV will usually be the first choice of treatment, provided there is some spontaneous respiration, relatively well preserved bulbar function, and of course acceptance by the child. Long-term nocturnal NIV was reported to be well tolerated in children suffering from various conditions such as neuromuscular disease, obesity-hypoventilation syndrome and cerebral palsy [31], with improvement in arterial oxygen saturation (S_{a,O_2}) and in P_{a,CO_2}, and with a compliance of >80%. BAROIS and ESTOURNET-MATHIAUD [51] also reported beneficial effects of respiratory assist in a mixed group of invasively and noninvasively ventilated children. In a recent study of 40 children aged 9 months to 16 yrs with different neuromuscular diseases, NIV *via* a mixture of nasal and full-face masks resulted in an increase in daytime P_{a,O_2} from 8.5±1.8 to 10.9±1.7 kPa, and a decrease in P_{a,CO_2} from 7.0±1.6 to 5.9±0.8 kPa [52]. Several small case series have supported these findings [29, 53, 54].

Specific conditions

Duchenne muscular dystrophy

Median survival is correlated to P_{a,CO_2}, minimal S_{a,O_2} and VC. A VC of <1 L has been shown to be the best single predictor of subsequent survival [55], which is 9.7 months following the development of daytime hypercapnia if respiration is not assisted [56]. Daytime hypercapnia and a base excess >4.0 mM has been found to be predictive of nocturnal desaturation [57]. Most studies have used positive-pressure ventilation (often BiPAP) *via* a nasal mask, but volume-cycled

ventilators have also been applied [41]. Negative-pressure ventilation has been reported [58] but has in other studies been associated with obstructive apnoeas [59]. Long-term preventive NIV in a randomised French study did not prove to be efficient. In fact, mortality was four times higher in the intervention group than in the control group. The study has been criticised though, and may not allow any firm conclusions [37]. LEGER *et al.* [60] demonstrated a 3-yr probability of continuing NIV in Duchenne muscular dystrophy (DMD) of 36%. Five (31%) progressed to ventilation *via* tracheostomy. SIMONDS *et al*. [61] showed a 1-yr survival of 85%, and a 5-yr survival of 75% using NIV exclusively, and a superior pulmonary function and survival was observed in a ventilated group of DMD compared to a nonventilated group after 2 yrs [56]. A recent study [62] showed significant improvements in nocturnal gas exchange after the use of NIV, but no changes in sleep architecture, respiratory muscle strength, in-hospitalisations nor in the need for invasive ventilation. Contrary to this, another study identified a reduction in hospitalisations in those treated with NIV compared with those treated *via* a tracheostomy [36]. Other studies have included DMD, but the data presentation does not allow firm conclusions [29, 31, 52].

Spinal muscular atrophy

SMA type II may require ventilatory support from the age of 2 to several years later in life. SMA type I has a 4-yr mortality of >80% [63]. NIV (initially Bird ventilator (Bird, Exeter, UK), later BiPAP) has been used predominantly, but volume-cycled mode has also been used. Successful pressure-targeted ventilators have been set at inspiratory/expiratory pressures of around 14/4 cmH_2O. Interfaces have included nasal masks and modified Hudson infant CPAP cannulae.

Gastric distension has been reported [63]. Maxillar hypoplasia from very early use of a nasal mask should be monitored. BAROIS and ESTOURNET-MATHIAUD [64] have for many years obtained favourable results from NIV in children suffering from SMA, as good in those below the age of 2 yrs as in those above that age. They have advocated respiratory support at an early age to improve rib cage development and foster lung growth [51]. Recently, 11 SMA type I individuals were reported to have been ventilated *via* the nasal route for almost 3 yrs [24]. Hospitalisations have occurred during intercurrent chest colds. Two were tracheostomised, one of which died later, and one was lost to follow-up. Two were being ventilated for 24 $h \cdot day^{-1}$. Another recent study [65], of four type IB SMA, reported NIV to eliminate sleep-disordered breathing, to improve sleep quality and symptoms (as indicated by the parents), to reduce heart rate and incidence and severity of infections after 1 yr. NIV was instituted for apnoea/hypopnoea index >5, transcutaneous carbon dioxide tension >6.7 kPa (50 mmHg), Sa,O_2 <90% for >20% of sleep time. Other studies including SMA have presented positive results for the long-term use of NIV, but have not detailed data to the degree that conclusions can be made [53, 66].

Parenchymatous conditions

With advancing cystic fibrosis, patients develop clinically significant hypoxaemia and hypercapnia, in particular during sleep [67]. NIV has been the preferred mode of ventilatory support to remedy these conditions [67–70]. BACULARD *et al.* [68] demonstrated in a case series of six persons (children and adolescents) that one patient gained weight, one showed increased FRC and two had more fluid sputum. Recently, GOZAL [67] found that NIV, contrary to oxygen alone, markedly improved alveolar ventilation during all sleep stages. Oxygenation improved while sleep architecture and arousals remained unchanged. Another study found an improvement in the subjective sensation of dyspnoea, in the quality of sleep and the capacity to perform activities of daily living [69]. Recently, pressure-support ventilation was shown to improve tolerance to chest physiotherapy as well as oxygenation during that treatment [70]. Leaks and gastric distension are reported [68], but would be expected to be similar to any other long-term ventilated group of patients. Prospective, randomised, controlled studies are needed to determine the effects of NIV, in particular its ability to act as a bridge to transplantation.

Central hypoventilation disorders

Nasal pressure-support ventilation has been the predominant mode reported, although the use of volume-cycled ventilators has also been reported [71]. When daytime respiratory insufficiency is present, tracheostomy is an option. A few studies [29, 71–74] have demonstrated beneficial effects such as improved oxygenation and ventilation from the long-term use of NIV in Ondine′s curse, including children from the age of 7 weeks to teenagers, who in the latter case have been converted from invasive ventilation.

Obstructive sleep apnoea

Generally this group of children does not suffer from hypoventilation, and thus, does not need genuine ventilatory support. Still, some will be in the border line zone and may benefit from bilevel ventilatory support. The prevalence of snoring in the general paediatric population is 7–12% [75, 76], and 10% of children who snore have significant sleep and breathing disorders [77], equivalent to 1–3% [78]. Untreated, some of the consequences are poor growth [79], followed by an increased weight gain velocity, a decrease in insulin-like growth factor [80], cardiac affection [81] and neurocognitive and behavioural disturbances [82], including poor school performance [83].

A multicentre survey [84] found an age distribution

in the use of CPAP in 94 patients as follows: 3% of the patients were <1 yr, 29% were 1–5 yrs, 36% were 6–12 yrs, and 32% were 13–19 yrs. Sixty-four per cent were males. Indications included obstructive sleep apnoea (OSA)-associated with obesity (27%), craniofacial abnormalities (25%) and idiopathic OSA persisting after adenotonsillectomy. Others [80] have reported improvement in OSA with respect to respiratory indices and sleep quality in a group of children suffering from achondroplasia. Significant improvement in respiratory parameters has also been demonstrated in children <2 yrs of age [85], and possibly the use of CPAP in infants with OSA is associated with a reversal of the putative depressing role OSA has on the arousal response in that population [86]. In a major study [33], compliance was reported to be ~75%. Recently, the American Academy of Paediatrics published guidelines on the diagnosis and management of childhood OSA syndrome, recommending that all children should be screened for snoring, that complex cases should be referred to a specialist, that PSG is the diagnostic gold standard, and that adenotonsillectomy is the first line of treatment. CPAP is an option for those who are not candidates for surgery or who do not respond to surgery [87, 88].

Family issues

The presence of a ventilator user will, to some extent, inevitably affect the ventilator user′s family. The impact will vary typically with how many hours per day the treatment is practiced [89], and it seems that NPPV is preferred to invasive ventilation, at least by attendants [90]. The accessibility and prevalence of attendants in relation to long-term ventilatory treatment of children with respiratory insufficiency vary considerably from one country to another. The effect of that on the family still remains to be elucidated. The quality of life scores in Duchenne boys ventilated noninvasively (as well as those ventilated invasively) have been reported to be equivalent to that of the general population, and highest for those living at home [91] and independent of the degree of progression of the disease [61]. Others tend to underestimate the quality of life of ventilator users [91]. Recently an adult population suffering from chronic alveolar hypoventilation due to neuromuscular or restrictive disorders, and who did not receive ventilatory assistance, was reported to have severely impaired health-related quality of life [92]. The effects of respiratory assistance on growth, development, cognition, social interaction and other activities in the child still awaits further research.

Conclusion

NIV in the paediatric population has become an option in the last few years, and is being applied increasingly. A few uncontrolled studies and case series indicate that the technique is useful for paediatric patients with a wide spectrum of respiratory disorders, including both hypercapnic and hypoxaemic conditions. The technique has proved effective both in the acute setting and in relation to long-term ventilation, with respect to improvement of arterial blood gases, survival and probably to quality of life. Adverse effects are generally minor, although in the chronic setting the effect of the interface on facial bony structures should be monitored closely.

Areas of future research should include: 1) generation of normative data and a much more detailed description of the immediate effects of noninvasive ventilation in various disorders; 2) techniques, in particular interfaces and triggering mechanisms; 3) comprehensive discharge plans, including structured training of parents and attendants; 4) instruments to measure quality of life in the various age groups and different disorders; 5) impact on development in the widest sense, *i.e.* pulmonary function, growth, cognition, social interaction; and 6) development of evidence-based guidelines for diagnosis, treatment, organisation and follow-up.

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