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Non-invasive positive pressure ventilation in children ☆

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ABSTRACT

Non-invasive positive pressure ventilation is increasingly used in children both in acute and in chronic setting. Clinical data supporting safety, efficacy and limitations in children are growing. Technical problems related to the ventilators performance and interfaces selection have not been fully resolved, especially for younger children. Non-invasive ventilation can be applied at home. Its use at home requires appropriate diagnostic procedures, accurate titration of the ventilators, cooperative and educated families and careful, well-organized follow-up programs.

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1. Introduction

An increasing number of children with chronic hypercapnic respiratory failure are currently treated with non-invasive ventilation [1]. Acute accesses to the emergency department or in-hospital follow-up controls of patients undergoing home long-term non-invasive ventilation are increasingly common occurrences [2–4].

Non-invasive ventilation has some undoubted peculiarities. By definition, it is a non-invasive technique, which can be applied on demand and preferably at night, causing less morbidity and discomfort [1,2]. It also allows preserving important functions such as swallowing, feeding, speaking, and coughing. Heating and humidification of the inspired air are greatly respected [5].

The introduction of non-invasive ventilation in pediatric practice has allowed the reduction of the number of children destined to tracheostomy, the limitation and/or the delay of the intubation of children with acute respiratory failure and/or exacerbation of chronic respiratory failure [5]; and also helped reduce the length of stay in the pediatric intensive care units of children who have been extubated and weaned from invasive ventilation in a shorter time [6]. Avoiding intubation prevents vocal cords or trachea damages, and reduces the risk of lower respiratory tract infections [7].

Non-invasive ventilation has also a better impact on quality of life of the patient with respect to the tracheostomy [5,10].

2. Definition, indications and objectives on non-invasive ventilation

There are two types of respiratory support: “invasive” and “non-invasive”. The distinction depends on the type of interface used for patient-ventilator connection. For non-invasive ventilation, gases are conducted into the airways via an external interface, in the case of invasive ventilation through an endotracheal tube or tracheostomy [2,10].

Non-invasive ventilation in children is indicated essentially for: 1) Diseases due to increased respiratory load (intrinsic cardiopulmonary disorders, abnormalities of the upper airways, especially skeletal deformities of the chest wall); 2) Disorders characterized by weakness of the respiratory muscles (neuromuscular diseases, spinal cord injuries); 3) Abnormal neurological control of ventilation (congenital or acquired alveolar hypoventilation syndrome) [2,5]. Main indications for non-invasive ventilation in children are summarized in Table 1. Authors' experience on non-invasive ventilation is shown in Fig. 1. Fig. 2 shows the increasing number of patient treated by non-invasive ventilation in the authors' institution since 1993.

Non-invasive ventilation can alleviate chronic respiratory failure through the correction of hypoventilation, the improvement of respiratory muscles function and reducing the workload of the respiratory system. An effective reduction of nocturnal hypercapnia by mechanical ventilation leads to an improvement of the daytime carbon-dioxide (CO_2), during spontaneous breathing [1]. According to Mehta et al. [10], objectives of non-invasive ventilation can be summarized into short and long-term goals. Short-term (including acute) goals are: relief from symptoms; reducing the work of breathing; improvement and stabilization of gas exchanges; optimization of the level of comfort; good patient-ventilator synchrony; minimization of risks; and avoiding intubation. Long-term goals are: improvement of the duration and quality of sleep, maximizing the quality of life, improvement of the functional status, and prolongation of survival.

3. Patient selection

Long-term non-invasive ventilation is not applicable to all children, as it requires a degree of cooperation, being more difficult to use in younger patients [2,5,10,11]. The ideal candidate for long term non-invasive ventilation should be a cooperative and in stable clinical condition patient [5,11]. Nocturnal or constant hypercapnia ($PaCO_2 > 55$–

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Table 1
Indications for NIV in children (modified from reference [11]).

Neuromuscular disorders
Duchenne muscular dystrophy
Spinal Muscular Atrophy
Nemaline myopathy
Abnormalities of the rib cage and chest wall
Progressive juvenile idiopathic scoliosis
Asphyxiating thoracic dystrophy (mild)
Advanced Cystic Fibrosis complicated by hypercapnia
Obesity-related disorders of ventilation
Prader–Willi Syndrome
Morbid obesity associated with obstructive sleep apnea
Overlap syndromes (obstruction of the upper airways and restrictive pulmonary dysfunction)
Spina bifida (pulmonary complications, Arnold–Chiari malformation, restrictive pulmonary dysfunction, obstruction of the upper airways)
Cerebral palsy (laryngeal dystonia and restrictive pulmonary dysfunctions)
Chronic obstruction of the upper airways
Obstructive sleep apnea complicated by hypercapnia
Down syndrome (maxillary hypoplasia, large tongue)
Craniofacial syndromes with midface or mandibular hypoplasia
Laringotracheomalacia
Chronic obstructive airways disease
Advanced Cystic Fibrosis
Disorders with central alveolar hypoventilation
Central Congenital Alveolar Hypoventilation Syndrome (CCHS)
Central Secondary Alveolar Hypoventilation
Rapid Onset Obesity with Hypoventilation, Hypothalamic, Autonomic Dysregulation Syndrome (ROHHAD)

60 mm Hg) should be present [11]. Indispensable prerequisite to its use is the presence of a certain degree of respiratory autonomy. Usually, it is applied at night and/or during daytime sleep (especially in younger children) [5]. Patients requiring ventilation throughout 24 h/day are usually not candidates for non-invasive ventilation [10,11].

4. Interfaces selection

The interface choice depends on the characteristics of the patient (age, facial characteristics, degree of cooperation, and severity of respiratory impairment). Regardless of the interface used, it is fundamental to limit the air leaks that may reduce the effectiveness of the ventilation [2].

In children, the interface acceptance is the first step for a successful non-invasive ventilation program. Interfaces should have good adhesion, a low resistance to airflow and should be light. The interface should exert less pressure on the skin that can be compatible with effective ventilation and the dead space volume should be minimized [1,11].

Many commercial interfaces are actually available for children. Nasal masks are the most often used interfaces, but there is getting a growing experience with oro-nasal and full-face masks [5,11]. Nasal pillows and mouthpieces are alternative options. In the authors' experience 93% of children use nasal-masks; 6% of children use oro-nasal or full-face masks; and the lasting 1% use other interfaces.

Transparent and with different form interfaces should be always used for each patient. The transparency facilitates a more easy and immediate inspection of the correct positioning [2,11]. The different forms reduce the risk of patient's discomfort, the development of side effects and facial deformities [5,11].

Accessories that allow keeping the interfaces in place are available for each type of them. A comfortable sealing, reducing the risk of air leakage, make them easier to use.

Helmet ventilation is a method that uses an interface consisting of a transparent helmet placed around the patient's head through which is possible to realize positive pressure ventilation. The helmet can be attached to the patient by axillary shoulder straps, waist belt and in the younger children through a "diaper" fixing system. Helmets are equipped with a protection system antisuffocation with automatic opening and a porthole airtight access to the patient [12].

5. Ventilators

Non-invasive ventilation in children can be performed with volume or pressure-targeted ventilators, according to the control variable through which the ventilator produces the inspiration [2,10]. A ventilator is in volume-controlled mode (volume-targeted ventilation) if the wave profile of the flow of gas delivered during inspiration does not change with changes in the compliance and resistance of the respiratory system [2,10]. The mechanical act generates a predefined volume of air or mixture of air/oxygen. A ventilator is pressure-controlled (pressure-targeted ventilation) if the wave profile of the pressure delivered during inspiration is not affected by changes in compliance or resistance of the respiratory system. The mechanical act generates a predefined pressure [2,10].

Some modern home ventilators provide both systems, and hybrid ventilations can be performed. Pressure-targeted ventilation is the most often used non-invasive ventilation modality [2,5,11]. It can be administered in various ways that can be characterized by being bound to strict parameters set by the physician, or flexible and modifiable by the patient himself by reason of its variable requests [10].

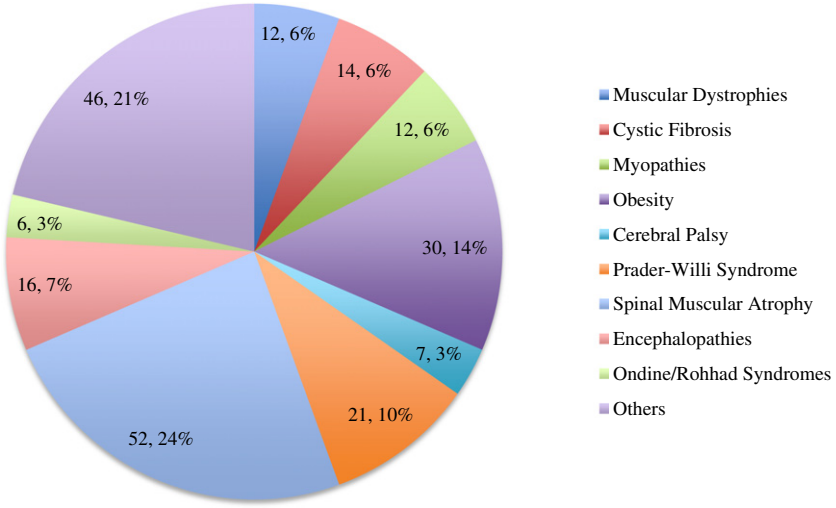

Fig. 1. Indications for non-invasive ventilation: authors' experience at Bambino Gesù Children's Research Institute (Rome, Italy).

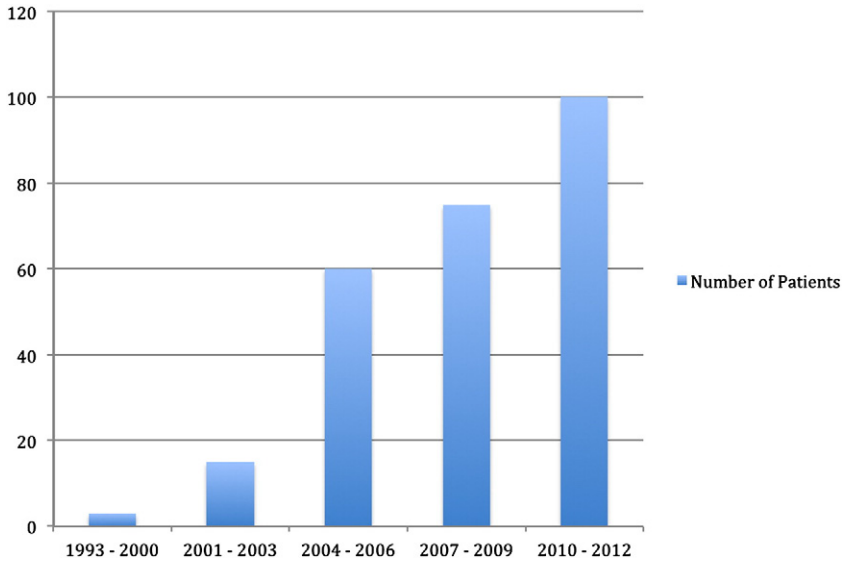

Fig. 2. Number of children initiated on respiratory support since 1993: authors' experience at Bambino Gesù Children's Research Institute (Rome, Italy).

Ventilators can be distinguished in bi-level, intermediate and critical care ventilators [13].

Bi-level ventilators typically provide pressure support or pressure control ventilation. Pressure applied to the airway is a function of flow and leak. For a given leak, more flow is generated if pressure setting is increased. They use a single-tube circuit with passive exhalation port. For a given pressure setting, more flow is required if leaks increases [2,10,13].

Intermediate ventilators are typically used for patient transport or home care ventilation. Many use a single-tube circuit with an active exhalation valve near the patient. These ventilators provide volume controlled, pressure controlled and pressure support ventilation. Their ability to compensate for leaks varies with different models [2,10,13].

Critical care ventilators are more sophisticated and with a variety of modes and alarms. They are designed mainly for invasive ventilation, but can be used for non-invasive ventilation. A major issue with the use of critical care ventilators for non-invasive ventilation is that many are leak intolerant, although newer generations feature non-invasive ventilation modes and some compensate well for leaks [2,10,13].

5.1. Ventilation modes

The present article will deal exclusively with pressure-targeted ventilation. Nomenclature for these modes varies between manufacturers, and this may generate confusion. For the pressure modes, some ventilators require selection of a pressure support level that is the amount of inspiratory assistance added to the pre-set expiratory pressure and is not affected by adjustments in positive end expiratory pressure (PEEP). Others require selection of peak inspiratory and expiratory positive airway pressures (IPAP and EPAP).

5.1.1. Continuous positive airway pressure (CPAP)

Continuous positive airway pressure does not actively assist inspiration and therefore is not a "true" ventilator mode [13]. Continuous positive airway pressure is a spontaneous modality with work of breathing entirely up to the patient [2,10,13]. Continuous positive airway pressure support is based on the delivery to the airways of a constant predefined pressure for the whole respiratory cycle. Continuous positive airway pressure acts by elevating the intraluminal pressure of the upper airway at levels higher than those of the critical transmural pressure that determines the collapse of the upper airway. This pressure keeps the airways open, promotes relaxing of the upper airway dilator muscles, and reduces inspiratory muscles activity of the upper airways and diaphragm [10,13]. Continuous positive airway pressure acts as an airways mechanical stent able to prevent the collapse of the pharyngeal airways, resulting in the increase in cross-sectional size of the upper airways mainly in the lateral direction and the thinning of the pharynx sidewalls. Its effect is negligible on the soft palate and the tongue. Continuous positive airway pressure prevents alveolar collapse pressure releasing a continuous additive flow. The consequent alveolar recruitments increase the functional residual capacity and counteract the development of atelectasis. Through this mechanism, CPAP improves oxygenation and downloading the inspiratory muscles reduces the work of breathing. In addition, by lowering left ventricular transmural pressure, CPAP may reduce afterload and increase cardiac output [2,5,10,13]. The pressures that are generally used in CPAP mode vary between 5–12 cmH_2O [14,15].

5.1.2. Bi-level positive airway pressure (Bi-level PAP)

Bi-level PAP provides respiratory support at two different levels. This method is based on the principle for which the pressure required to maintain the airway patency is different within the same respiratory cycle and requires higher values in the inspiratory phase and minors in the expiratory phase [5]. Using bi-level PAP is possible, therefore, to adjust separately a lower expiratory positive airway pressure (EPAP, CPAP, PEEP) and higher inspiratory positive airway pressure (IPAP, PIP).

The mechanical ventilator has a motor–generator, usually a turbine, which is able to supply a very high flow. This flow is inserted in the patient's inspiratory act amplifying and improving its effectiveness. The inspiratory pressure, therefore, enhances the patient's spontaneous inspiratory act, and should, therefore, be delivered as synchronous as possible with the patient's respiratory efforts [2,10,13].

The task of the clinician is to determine the extent of the work exerted by the mechanical ventilator and the level of pressure must be set to reach this goal [5].

Expiratory pressure, when used with a circuit provided with adequate exhalation port, allows: eliminating more easily exhaled air; and preventing the re-breathing of CO_2. As already discussed for CPAP, the EPAP helps keeping the upper airways open; favors the recruitment of alveoli and pulmonary districts; increase the functional residual capacity; and reduce the tendency to micro- and macro atelectasis [2,5,10,13].

The tidal volume will be generated as the result of the delta between these two pressures within certain limits (usually 15 cmH_2O) [16], the

flow resistance of the ventilator circuit, any airflow limitation and the compliance of the chest wall and lungs [5,13].

Usually, the inspiratory pressure is adjusted between 6–14 cmH_2O [2,10]. The main goals of increasing the IPAP are to achieve a tidal volume of 6–10 mL/kg of ideal body weight, decrease the work of breathing (trough a lesser use of accessory muscles), decrease the respiratory rate, and reduce the $PaCO_2$ [2,5,10,13].

It is recommended a minimum level of EPAP of 3–5 cmH_2O [17]. The main goals of increasing the EPAP are to eliminate upper airway obstruction, to reduce the intrinsic positive end-expiratory pressure (PEEPi), and to improve oxygenation [18].

To keep the same pressure support, when EPAP needs to be increased, the IPAP should be increased too. This adjustment maintains unchanged the delta between inspiratory and expiratory pressures [16].

Bi-level positive pressure ventilation can be performed in two different modes: Pressure Support Ventilation (PSV) and Pressure Control Ventilation (PCV) [2,5,10,13].

In PSV mode, the ventilator ensures a maximum value of inspiratory pressure in the airways equal to that set by the operator. This pressure support allows the patient to achieve more effective breaths. The patient determines respiratory rate, inspiratory flow and inspiratory time by determining the onset of inspiration, muscle strength applied during the inspiration and passage to the expiration [13].

The use of the PSV mode allows preserving the patient's spontaneous breathing while ensuring the reduction of excessive work of breathing undergone by the patient. The patient's inspiratory drive activates a "trigger" that drives the pressure support for the inspiration. Once the inspiratory trigger has been activated, the ventilator provides the pressure level chosen and keeps it until the patient's inspiratory activity ceases. Pressure support ventilation provides a flow-dependent inspiratory time variable as a function of the resistance and compliance of the respiratory system; the level of intrinsic positive end-expiratory pressure (PEEPi); and the activity of the inspiratory muscles of the patient [2,10,13].

This mode is preferable in patients capable of spontaneous breathing and able to activate the ventilator cycles. On the contrary, it is not recommended for patients with severe depression of consciousness or with significant impairment of the muscle pump efficiency or ventilatory drive [17,18].

Pressure support ventilation prevents atrophy from disuse of the respiratory muscles, and favors the lower use of sedation, the lowest risk of hemodynamic side effects, a better distribution of tidal volume and ventilation/perfusion ratio [13,17,18].

Pressure support ventilation can be performed in spontaneous or spontaneous/timed (S/T) mode. In the spontaneous mode the ventilator is triggered by the patient, the respiratory acts are supported (limited) by the ventilator, and cycled in expiration by the patient. In the spontaneous/timed mode, a combination of supported spontaneous breathing and mechanically generated acts will be possible. If the patient's spontaneous respiratory rate is lower than the pre-set (back up rate), mechanical acts are triggered, limited and cycled by the ventilator. Ventilator cycles in expiration when it senses a fall in inspiratory flow rate below a threshold value, or at a pre-set time [13].

In PCV mode, the operator sets the maximum level of pressure that is delivered by the ventilator for the duration of the inspiratory act, the respiratory rate and the inspiratory:expiratory ratio (I:E), in the absence of respiratory effort. Breaths delivered by the ventilator are determined by a pressure, duration of inspiration and expiration default. Key parameter is the derived tidal volume that depends on the ratio between inspiratory pressure, inspiratory time and mechanical properties of the lung–thorax system [13].

Triggering by the patient is allowed, but the ventilator delivers a respiratory act identical to the pre-set respiratory act. This mode of ventilation is defined assisted/controlled (A/C) for which a combination of assisted spontaneous breathing and controlled acts will be possible if the spontaneous respiratory rate is lower than the pre-set (back up rate) [13].

This mode is preferable in severely ill patients with significant impairment of the muscle pump efficiency or ventilatory drive [13,17,18].

6. Technical aspects

6.1. Triggers

The sensors that allow starting the mechanical ventilator breath and finishing it on the basis of the patient's respiratory efforts are called "triggers".

There are various types of triggers. Briefly, in the "volume trigger" system the patient has to move a certain amount of air to determine the start of the respiratory act by the mechanical ventilator; in the "pressure trigger" system a modification of the pressure in the circuit determines the triggering of inspiration; and in the "flow trigger" system within the breathing circuit is maintained a flow of gas, the inhalation of the patient determines a change in the flow and the start of inspiration [2,13].

There are some issues related to the inspiratory trigger. In the "wasted effort" phenomenon, the initiation of the act failed due to lack of sensitivity of the trigger. This entails attempts to breathe by the patient which are not associated with start-up aid by the mechanical ventilator. In the "autocycling" phenomenon, the mechanical ventilator provides automatically triggered respiratory acts even in the absence of a request by the patient. This event is determined by excessive trigger sensitivity [2,13].

6.2. Synchrony

The termination of the inspiratory act is called "expiratory cycling". Clinician can set the length of time of the inspiratory time (time cycling). Patient can alternatively determine the passage from inspiration to expiration, causing the end of the act of the mechanical ventilator (flow cycling). In this case, the mechanical ventilator is sensitized for the reduction of the inspiratory flow that occurs at the end of the patient inspiration, and the occurrence of a certain variation of the flow allows the exhalation [2,10,13].

Defects may occur in the expiratory flow cycling, especially if the mechanical ventilator, usually due to air leaks, does not recognize the end of the inspiration. In this situation, the mechanical ventilator continues to inflate while the patient tries to exhale. This phenomenon is called "hung up" and can be very annoying for the patient. There can be remedied by setting inspiratory time limit beyond which if flow cycling does not occur time cycling occurs [2,10,13].

6.3. Circuits

The patient circuit includes all the components that carry the gas from the ventilator to the patient and return the patient's exhaled gas to the environment. Apart from conduction device, the circuit also performs gas filtering and humidification. The interfaces are connected to the ventilator through dedicated circuits within which passes the airflow.

The circuit can be "single-tube" (the air passes during inspiration and during expiration) or "double-tube" (with this configuration, inspiratory and expiratory gases are separated: one for the passage of air during inspiration and the other for the passage of expiratory air).

For critical care ventilators, double-tube circuits are used, and these are provided with inspiratory and expiratory valves. The expiratory valve actively closes during inspiratory phase and the inspiratory valve closes during expiratory phase. The expiratory valve is usually incorporated into the ventilator. For intermediate ventilators, a single-

tube circuit is used with an exhalation valve near the patient. The expiratory valve is actively closed during the inspiratory phase to prevent loss of delivered tidal volume. During exhalation, the expiratory valve opens and the inspiratory valve closes. Because the expiratory valve is near the patient, rebreathing is minimized. For bi-level ventilators, a single-tube circuit is used. A leak port, which serves as passive exhalation port for the patient, is incorporated in the circuit near the patient or into the interface [13].

Non-invasive home ventilators are usually equipped with a single tube. The circuit can be provided with a "non-rebreathing" exhalation valve. This valve allows the non-rebreathing of CO_2 eliminating all the exhaled air. Alternatively the circuit can be free of the expiratory valve, but provided with a CO_2 dispersion system [13]. The latter is typical of the bi-level ventilators and three different variants are available: 1) the CO_2 is carried out through a hole in the mask; 2) circuit provided with a dispersive expiratory system (whisper swivel connector); and 3) circuit provided with a unidirectional expiratory system (plateau valve).

Although certain types of circuit can be sterilized and reused, most of them are made with disposable material.

6.4. Humidification

Systematic humidification of the ventilator gas is not necessary for non-invasive ventilation. However, in order to avoid the excessive dryness of the upper airways which can determine increased resistance of the respiratory system, humidification in the circuit can be supplied [5].

Some home ventilators are equipped with heated humidifier system. Often, the system has to be interposed in the circuit. Its presence can increase the circuit resistances, interfere with the ventilator triggering, and increasing the dead space, may have effects on the pressure release [2,5].

For these reasons it is necessary to accurately monitor the effectiveness of the non-invasive ventilation on the work of breathing and gas exchanges whenever changes are made to the circuit [2,5].

Commercial humidification systems include non-heated-wire humidifiers, heated-wire humidifiers, and heat and moisture exchangers (HMEs). HMEs' use should be limited to short-term mechanical ventilation sessions [2,10,13].

6.5. Oxygen supplementation

Carbon dioxide should be minimized first by ventilator use before considering oxygen therapy. It is also important to remember that supplemental oxygen is not a replacement for assisted ventilation in patients with hypoventilation [5].

The oxygen concentration of the inspired gas may be enriched with different modes. A simple and safe method is to introduce 100% oxygen at low flow through a door located on the nasal or facial mask. The advantage of this method is that a relatively low flow of oxygen may be sufficient and there are no interruptions in the circuit between the interface and ventilator. The disadvantages of this method are the inability to accurately measure the FiO_2 and not adequate humidification [2,5,10,13,17,18].

An alternative is represented by the provision of a high flow of 100% oxygen introduced through a connector inserted into the circuit near the patient's interface. Using this method of enrichment can be achieved with FiO_2 values ranging from 40% to 55%. The disadvantage of this approach is that it does not respect the integrity of the circuit manufacturer's guidelines and high-flow oxygen is needed to reach the desired FiO_2 [2,5,10,13,17,18].

Some modern ventilators can be directly connected to the source of O_2. With such devices, high FiO_2 percentages and continuous FiO_2 readings can be obtained [2,10,13].

7. Non-invasive ventilation timing

Non-invasive ventilation in children is usually a consequence of the following situations:

- Inability to wean the child from mechanical ventilation began to treat an acute respiratory failure,
- Re-exacerbation of a chronic respiratory failure,
- Slow progression towards different degrees of hypercapnic respiratory failure,
- Sleep disorders of breathing with hypercapnia [5,11,13].

8. Non-invasive ventilation initiation

If non-invasive ventilation can be established gradually, a clinical session aimed at the introduction of the patient and family to its practice must be planned [5].

Non-invasive ventilation training should start by using very low pressures and when the patient continues to tolerate pressures throughout the night, the pressures can be gradually increased [5,11].

The choice of pressures is the process by which the clinician searches for a compromise between defect correction (through the increase in pressures), and the limitation of the side effects (with the use of a pressure as lower as possible, but still effective) [5,11].

Pressure requests depend on the individual patient's current clinical condition and must be obtained from the evaluation of its monitoring [5,11,20].

The families must be highly motivated and supportive and this greatly increases the success of the non-invasive ventilation institution [5,17,18].

9. Monitoring

Accurate monitoring during non-invasive ventilation is very important to ensure its effectiveness and safety. The level and type of monitoring should be proportional to the patient's clinical condition [2,10].

For patient being treated acutely, in-hospital continuous monitoring is indicated with a pulse-oxymeter or a multichannel cardio-respiratory monitor. A strict clinical observation is also mandatory and it must always assess patient's comfort, respiratory rate, level of dyspnoea, oxygen saturation, signs of possible patient-ventilator asynchrony, intolerance to interface, air leaks, gastric distension, dry eyes, and damage to the facial skin. Arterial blood gas analysis should be assessed after 1–4 h after the non-invasive ventilation establishment and 1 h after each modification of the ventilator setting or FiO_2 concentration [2,10].

In some cases other parameters including electrocardiogram and expired tidal volume may be considered [2,5,10,11].

For patients being treated with non-invasive ventilation electively, once a good patient's tolerance is reached, a titration study must be performed in order to optimize ventilator pressures [21]. According to the local diagnostic availabilities, a polysomnography, a cardio-respiratory sleep study or a nocturnal non-invasive monitoring of oxygen saturation (SpO_2) and carbon dioxide (CO_2) should be performed [17–19].

Either for first titration and/or for follow-up titration studies, sleep monitoring can be performed as follow:

- Two separate nights: first night for *baseline* sleep study recording during spontaneous breathing; second night *during non-invasive ventilation* sleep study recording.
- Single night: sleep study is divided (*split night*) into two different parts (during spontaneous breathing and during non-invasive ventilation) [21].

9.1. Polysomnography

Polysomnography (PSG) in a sleep laboratory represents the gold standard for the diagnosing of sleep disorders of breathing. Polysomnography should be performed as follow: at least six EEG channels (Fp1-A2, Fp2-A1, C3-A2, C4-A1, O1-A2, and O2-A1 electrode placement according to the international 10–20 system), left and right electrooculogram (EOG), chin electromyogram (EMG), electrocardiogram (ECG), electromyogram of the left and right tibialis anterior muscles, nasal cannula, thoracic and abdominal respiratory effort, and oxygen saturation, and end-tidal or transcutaneous CO_2 monitoring (see below). Polysomnography is a costly and time-consuming procedure and sometimes of difficult clinical application due to limited availability and long waiting list [1,7]. To obviate this important issue, cardio-respiratory sleep studies are increasingly used abbreviated testing [8–11]. Cardio-respiratory sleep studies are based on the same full PSG channels with the exception of the EEG [22].

9.2. Pulse-oximetry

The estimation of arterial hemoglobin oxygen saturation (SpO_2) by pulse oximetry is based on the specific characteristics of oxygenated and deoxygenated hemoglobin (oxyhemoglobin and deoxyhemoglobin, respectively) with regard to light absorption in the red and infrared spectra. By calculating the ratio of red and infrared spectra absorption ratios, the percentage of oxyhemoglobin can be calculated. The performance of each device is strictly related to the complexity of these algorithms and to the speed and quality of the microprocessor. The probe of the device must be positioned in such manner that the emitter and the detector are exactly opposite to each other with 5 to 10 mm of tissue between them. The performance of pulse oximeters deteriorates remarkably when SpO_2 decreases to <80% [23]. Limitations of pulse oximetry include erroneous readings related to motion artifact, dark skin pigmentation, irregular heart rhythms (especially tachyarrhythmias), and electromagnetic energy interferences. Lower SpO_2 readings might occur when the probe is inappropriately placed, especially on the small fingers of neonates and infants. Intense white or infrared light might interfere with pulse oximetry and lead to falsely low SpO_2 readings. Abnormal or variant hemoglobin molecules might interfere with pulse oximetry and lead to inaccurate results that might influence clinical decision-making [23].

9.3. Non-invasive carbon dioxide monitoring

Carbon dioxide monitoring can be helpful for clinicians to make diagnosis of specific medical conditions, leading to important treatment decisions. Carbon dioxide monitoring can also be helpful for the managment of patients receiving oxygen supplementation. Non-invasive CO_2 monitoring can be performed by end-tidal and transcutaneous CO_2 techniques.

The technique of end-tidal CO_2 is based on the detection of end-tidal CO_2 by capnography. An inherent property of CO_2 is to absorb infrared radiation at a very specific wavelength. Capnographs contain sensors that produce infrared sources of blackbody radiation at these wavelengths. These sensors enable the calculation of CO_2 levels in a breath sample. This method allows detection of the breath-by-breath CO_2 values obtained from an expiratory plateau.

Capnographs measure CO_2 concentration using either mainstream or sidestream configurations [24].

In mainstream configuration, the capnograph sensor is located on a special airway adapter so that CO_2 is measured directly in the patient's breathing circuit. The main drawbacks of these methods are the weight of the sensor on the airway, the external positioning of the sensors that make them vulnerable to damage, and the inability to monitor non-intubated patients easily [24].

In sidestream configuration, a sample of exhaled breath is aspirated from the breathing circuit to a sensor residing inside the monitor. Sidestream configurations are appropriate for both intubated and non-intubated patients. The drawbacks of sidestream include the management of liquid and secretion into the device's circuit and the need for large breath sample rate for an accurate CO_2 reading [24].

Microstream is a newer capnograph configuration. Microstream improves conventional sidestream technology because there is no sensor at the airway. It can work for both intubated and non-intubated patients of all ages. Microstream uses laser-based molecular correlation spectroscopy as the infrared emission source. Microstream uses a breath-sampling rate of 50 mL/min and this is useful for patients of all ages, including neonates [24].

The other CO_2 non-invasive detecting system is the transcutaneous technique. With this method, CO_2 values can be detected through a skin sensor. The core of the sensor is a silver cylinder, in which a heating element and temperature sensors are embedded through the silver cylinder passes a fine platinum wire, which forms part of the pO_2 sensor. At the surface of the silver cylinder there is a solid-state pH sensor. A thin electrolyte layer is held in place over the slightly convex silver cylinder by tightly stretched membranes. The membrane material is permeable to O_2 and CO_2. Oxygen and CO_2 outside the sensor diffuse across the membrane into the electrolyte. A tiny current is generated which is proportional to the pO_2, the sensor is exposed and CO_2 diffusing into the electrolyte changes its pH depending on the pCO_2 to which the sensor is exposed. The transcutaneous sensor can measure both the pO_2 and pCO_2 at the membrane surface. Over time, the sensor changes its sensitivity, so frequent calibration is required [25].

The correlation between the transcutaneous ($TcPCO_2$) and arterial ($PaCO_2$) CO_2 may be influenced by the various clinical conditions or factors as: positioning above superficial large caliber veins or damaged skin areas or edema; patient's inadequate site of monitoring; inadequate contact between patient's skin and sensor, and presence of shunts. Transcutaneous PCO_2 readings are typically overestimated if the monitoring site is hypoperfused. Transcutaneous PCO_2 readings can be underestimated if the patient presents abundant subcutaneous fat deposition [25].

Compared with capnography, the transcutaneous methods provide more slowly CO_2 values reading. It is helpful especially with ventilated patients, because of the sensor positioning is outside the patient's airways/ventilator circuit line [24,25].

10. Enter the patient on at home long-term non-invasive ventilation program

Sending the patient home with a long-term non-invasive ventilation program needs a series of steps. An accurate non-invasive ventilation training session should take place in a pediatric comfortable environment [11]. An assessment of the clinical and respiratory function stability should be performed for a safe use. Before discharge a comfortable interfaces selection should be carried out. A detailed and personalized follow-up plan set in proportion to the child's stability level must be provided. Prior to discharge, the patient's respiratory status should be stable on the same ventilator and circuit which the child will use at home, at least for several days. Home equipment must be evaluated in each child prior to discharge [5,11,17,19].

The use of home non-invasive ventilation requires appropriate diagnostic procedures, accurate titration of the ventilator, cooperative and educated families and a careful, well-organized follow-up programs [5]. An easy access to the reference center should be also provided. A team of experts should follow children undergoing long-term non-invasive ventilation [11].

Although the optimal frequency for follow-up evaluations has not been determined, these evaluations should generally be performed more frequently in infants and small children with rapid growth [5]. On such occasions should be re-considered the history and a

complete clinical assessment. Interfaces and instrumentation must be re-evaluated. The management of the interfaces provides a regular reassessment of the proper fitting; a careful control of the interface's pressure site; and periodic change in the position or shape [11,17]. The circuit integrity and correct positioning and functioning of the heated humidifier should be always reassessed. Ventilator alarms must be always verified, and problems detected at home should be discussed with patients, parents or caregivers. Compliance should be systematically controlled through the internal memory of the instrument to verify the actual time of ventilator use. This check also allows assessing air leakages, and evaluating pressures delivered and SpO_2 values [5,11].

Pulmonary function tests (according to the age and the patient' underlying disease) should be performed. Arterial or capillary blood gases analysis must always be performed. Chest x-ray and lateral projection of the skull must be periodically repeated [5].

Polysomnographic evaluations are recommended before initiating non-invasive ventilation, before discharging with the ventilator, and during each in-hospital follow-up admission. Nocturnal polysomnography (see above for technical details) should be performed in order to re-evaluate the effectiveness of the proposed treatment or to make any changes correlated with a progressive clinical deterioration or the natural progression of the underlying disease. The examination should provide the recording of pressure at the interfaces, air-leaks and patient/ventilator synchronization. Pressure requests may change over time as a result of the growth of the patient and/or the evolution of the disease [5,19,21].

Echocardiography should be performed annually for the evaluation of the function of the right ventricle, for the estimation of the pressure in the pulmonary artery and the search for any tricuspidal regurgitation [11].

Normocapnia may not be a realistic goal in some patients, therefore the clinician must always balance its decisions between non-invasive ventilation effective but “comfortable” and the risk of a reduced adherence that is much more likely with the selection of high pressures [5,11].

11. Complications and contraindications

In children are not reported serious complications with the use of non-invasive ventilation and adverse effects described are minor [10].

Problems of compliance may occur due to nasal symptoms such as excessive dryness, congestion, rhinorrhoea or epistaxis. These symptoms can be prevented, reduced or resolved through the humidification and heating. Abdominal distension is an uncommon problem [1,2]. One case of a cerebral air embolism complicating bi-level ventilation has been reported in a 13-year-old boy presenting a post-bone marrow transplant pneumonitis [26].

The mid-facial hypoplasia has been described mainly in patients who started non-invasive ventilation earlier in life. This condition may result in physiognomic changes, orthodontic problems and generate or worsen obstructive sleep apnoea. Monitoring of maxillo-mandibular growth is necessary in infants, younger children or in those children receiving long-term non-invasive ventilation. In these cases, it is mandatory to regularly change the pressure point of the interface to prevent mid-face hypoplasia [27].

Inhalation is a potential complication in children and its risk is theoretically greater when using a face-masks in a child unable to protect himself quickly removing the mask by itself [1,2,10].

Contraindications to NIV are recent pneumothorax, facial trauma or burns, recent upper airway or digestive tract surgery [2,10,11].

12. Conclusions

Non-invasive ventilation in children is increasingly used both in acute and chronic settings. The clinical data supporting its application, safety, efficacy and limitations are currently growing. Some issues with ventilators' performance and the interfaces availability especially for infants and younger children, still remain partially unresolved. Non-invasive ventilation can be applied at home, with useful implications on the psychosocial development of the patient, the family functions and costs. Long-term non-invasive ventilation requires proper diagnostic procedures; accurate titration of the ventilators; cooperating families; and well-organized follow–up programs.

Conflict of interest

The authors have no conflict of interest to report.

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