Abstract NonInvasive Ventilation (NIV) provides ventilatory support without the use of an invasive artificial airway device. Compared to invasive ventilation, NIV reduces the risk of infections, prevents tracheal injury and diminishes the use of sedatives and analgesia. The physiological benefits from NIV are similar to invasive ventilation, providing reduced work of breathing and improving gas exchange. In selected patients, NIV has been increasingly used to serve as an alternative to intubation. Compared to invasive ventilation, NIV improves survival and reduces complications in selected patients with acute respiratory failure. Main indications for NIV therapy are exacerbation of chronic obstructive pulmonary disease, cardiogenic pulmonary edema, acute respiratory failure in immune-compromised patients and prevention of respiratory failure after extubation. NIV may also have other, less well-described clinical applications, such as in the postoperative setting. NIV shall not be used when patients cannot protect their airway or possess other contraindications for noninvasive ventilation. The success of NIV critically depends on the correct patient selection, the expertise of the team applying it and the type of interface used. In general, NIV is considered safe with most complications being related to interface intolerance. The design of the interface is therefore critical to the success of the noninvasive ventilation. Ambu provides various types of NIV interfaces, all designed to optimize patient comfort and minimize air leaks to ensure success of the NIV therapy.

THE RESPIRATORY SYSTEM AND NONINVASIVE VENTILATION

The Process of Ventilation
The primary function of the respiratory system is to exchange oxygen and carbon dioxide. Ventilation is the process by which air moves in and out of the lungs thereby allowing air to be exchanged between the atmosphere and the blood. Inhaled oxygen enters the lungs and reaches the alveoli, the tiny hollow sacs constituting the final branching of the respiratory tree. The surfaces of the alveoli are covered with small blood vessel, the capillaries. During ventilation, oxygen is inhaled into the lungs and passes from the alveoli into the bloodstream through which it is distributed to all the organs and cells of the body. Carbon dioxide, a waste product from the cells, passes from the capillaries through the alveoli wall into the lungs where it is breathed out during ventilation (1). Normal inspiration is initiated when the diaphragm muscle and the intercostal muscles contract, resulting in the thorax to enlarge which in turn forces the lungs to expand. The enlargement of the lungs causes the pressure inside the lungs to drop to less than the pressure of the surroundings thereby causing a bulk flow of air from the atmosphere through the airways into the alveoli. At the end of inspiration, the diaphragm muscle and the intercostal muscles relax which in turn causes the thorax and the lung to passively return to their normal dimension forcing the air out of the alveoli and into the atmosphere (1, 2).

Acute respiratory failure is a condition in which pulmonary function is markedly impaired, usually characterized by elevated carbon dioxide or decreased oxygen (or both) in the arterial blood. Acute respiratory failure may e.g. result from acute diseases of the lung such as cardiogenic pulmonary edema characterized by fluid filling, or collapse of the alveoli leading to impairment in the gas exchange during ventilation. Through the promotion of pulmonary gas exchange, noninvasive ventilation can be used in a wide range of disorders that lead to acute respiratory failure (2, 3).

Noninvasive Ventilation Modes
Noninvasive ventilation (NIV), often also referred to as Noninvasive Positive-Pressure Ventilation (NIPPV), is the administration of ventilatory support without using an invasive artificial airway (an endotracheal tube or a tracheostomy tube). NIV is delivered through an interface, typically a facial or a nasal mask, which connects the patient’s airway to the ventilator tubing (4). Bilevel Positive Airway Pressure (BiPAP) is the most commonly used modality of NIV. BiPAP supports breathing and provides two levels of positive pressure: A high inspiratory positive airway pressure and a lower expiratory positive airway pressure (5). Continuous Positive Airway Pressure (CPAP) is a ventilation mode which provides a constant pressure in the airway, both during inspiration and expiration. Although CPAP does not actively assist inspiration as do other forms of NIV, CPAP is often classified as a NIV mode in the literature (4, 6). Like BiPAP, the positive pressure during expiration ensures the opening of collapsed alveoli, which in turn enhances gas exchange and oxygenation. However, CPAP does not actively aid the inspiration phase as BiPAP. CPAP is a relatively simple technique compared to BiPAP which is a more complex mode demanding much more expertise from the health personal applying it (5).

In the present review, the specific type and mode of NIV is not always specified in the described applications. NIV may represent BiPAP, CPAP or other noninvasive modalities unless otherwise specified.
APPLICATIONS OF NONINVASIVE VENTILATION

In Europe, the rate of use of NIV in Intensive Care Units (ICUs) is about 35% of ventilated patients and higher in respiratory intensive care units or emergency departments. In North America, NIV is begun most often in emergency departments with most patients subsequently transferred to ICUs (6).

The current review presents the clinical applications of NIV having broad acceptance and a solid documentation for the clinical performance. However, the list of applications of NIV in the hospital setting presented here is not exhaustive. Additionally, applications of NIV in the domestic setting, e.g. in the treatment of sleep apnea, are not included in the present review.

Noninvasive Ventilation of Patients with Exacerbation of COPD

Chronic Obstructive Pulmonary Disease (COPD) is an umbrella term for patients with chronic bronchitis, emphysema, or both. In patients suffering from COPD, the airflow to the lungs is restricted. Smoking is the major cause of COPD. Exacerbations, the acute worsening of COPD symptoms, include increased breathlessness often accompanied by increased cough and sputum production, wheezing, chest tightness and fever. The dominant clinical feature in COPD is impairment of expiratory airflow (3).

NIV is currently the first-line treatment in the initial management of patients with acute respiratory failure due to COPD exacerbations (7). Several randomized controlled trials have shown that the addition of NIV to the medical treatment of COPD exacerbations relieves dyspnea, improves vital signs and gas exchange, prevents endotracheal intubation, lowers mortality and shortens the time spent in the hospital. The literature indicates that NIV should primarily be used for the early treatment of COPD patients with mild-moderate respiratory distress to avoid further deterioration and thus avoid endotracheal intubation (6, 7).

Noninvasive Ventilation of Patients with Cardiogenic Pulmonary Edema

During pulmonary edema, excess fluid accumulates in the alveoli in the lungs. The presence of excess fluid in the alveoli reduces gas exchange and results in difficulty of breathing and poor oxygenation of the blood. In cardiogenic pulmonary edema, the edema is due to failure of the heart to remove blood from the lung circulation (2). The use of NIV in patients with cardiogenic pulmonary edema is supported by multiple randomized trials (7, 8). The main physiological benefits from NIV in these patients are likely due to an increase in functional residual capacity that reopens collapsed alveoli and improves oxygenation. This also increases lung compliance and reduces work of breathing. Several meta-analysis have shown equivalent reductions in intubations and mortality rate with CPAP and BiPAP for cardiogenic pulmonary edema. Thus both CPAP and BiPAP can be used to treat cardiogenic pulmonary edema with equal expectations of success. Some recommend starting with CPAP because it is simpler. If patients remain dyspneic or hypercapnic on CPAP alone, BiPAP may be initiated (7, 8). Together with exacerbations of COPD, acute pulmonary edema is the most common indication for NIV therapy (6).

Noninvasive Ventilation of Immuno-Compromised Patients with Respiratory Failure

Immuno-compromised patients have a suppressed immune response due to e.g. the administration of immunosuppressive drugs after transplantation or due to certain disease processes such as Acquired Immune Deficiency Syndrome (AIDS). Because the immune system has a reduced ability to fight infections, infectious complications are a common problem in these patients. Prevention of health-care associated infections, e.g. pneumonia resulting from the use of invasive intubation, is therefore an important factor in the treatment strategy of immune-compromised patients. Randomised controlled trials demonstrate that NIV treatment of respiratory failure in patients having received solid-organ or bone-marrow transplants, results in decreased intubation rates, decreased mortality rates and shorter ICU lengths of stay when compared to conventional therapy. Similar findings have been reported for AIDS patients. The reduced mortality was considered to be related to a reduced number of infectious complications associated with NIV compared to invasive ventilation, including ventilator-associated pneumonia and other nosocomial infections (4, 6, 7).

Noninvasive Ventilation During Weaning

In the majority of cases, ventilation through an endotracheal tube can be withdrawn immediately after significant improvement of the underlying indication for the invasive ventilation. However, in approximately 25% of patients, gradual withdrawal of ventilatory support, called weaning, is required (9). Extubation, the process of removing the endotracheal tube from the patient’s airway, may be a major challenge especially in patients with chronic respiratory disorders such as COPD. Persistent weaning failure is associated with prolonged invasive mechanical ventilation and increased mortality. NIV has been used to treat respiratory failure after extubation and to prevent acute respiratory failure during weaning. However, the clinical evidence for the use of NIV in the treatment of respiratory failure after extubation is not substantial and in some circumstances it appears to be unfavorable. One study suggests that NIV delayed necessary reintubation in patients developing respiratory failure after extubation, with the consequent risk of fatal complications (4, 10). The scientific evidence is more favorable for the use of NIV in the prevention rather than in the treatment of respiratory failure after extubation. In certain subsets of patients whose clinical characteristics at the time of extubation may predict re-intubation, NIV may prevent post-extubation respiratory failure. Two randomized trials were performed to assess whether NIV was effective in preventing the occurrence of post-extubation failure in patients at risk (11). Both studies, which adopted similar criteria to define patients at risk and had comparable study designs, showed that the groups treated with NIV had a lower rate of re-intubation than did the groups in which standard therapy was used. Furthermore, in one of the two studies, mortality was also reduced in the subgroup of patients treated with NIV (11). This suggests that, when promptly started, the use of NIV in selected patients “at risk” may prevent post-extubation respiratory failure.

Noninvasive Ventilation for Postoperative Ventilatory Support

Major abdominal and thoracic surgeries are often complicated postoperatively by respiratory failure. Pulmonary atelectasis, the collapse of lung tissue reducing gas exchange in the alveoli, is a frequent complication after major surgery and may predispose patients to pneumonia. In randomized clinical trials, NIV reduced atelectases and prevented pneumonia more effectively than standard therapy after upper abdominal surgery. Moreover, NIV substantially improved gas exchange after gastropasty in obese patients (6). Preventive use of NIV for a week before or immediately after thoracic, cardiac or vascular surgeries may reduce loss of lung volume. Thus data exists that may support the use of NIV in the postoperative setting. However, more data from randomized controlled clinical trials are needed before specific recommendations can be made (6).
SELECTION OF PATIENTS

When selecting patients for NIV therapy, clinicians must identify those in need of ventilatory assistance and screen out those with mild respiratory insufficiency who can be managed with medical therapy alone (12). The clinician must exclude, among those needing ventilatory assistance, those in whom NIV would be unsafe and who should be promptly intubated. A patient’s ability to protect the airway, e.g. by having an adequate ability to cough, is one of the most important considerations when making this determination (12). Contraindications for NIV include, among others, inability to protect the airway, respiratory arrest, medical instability, excessive secretions, agitation, lack of cooperation and inability to fit the mask. Although NIV is ideally used for periods of a few hours to a few days in patients with reversible causes for their acute respiratory failure, there are many examples of patients who have had favorable outcomes after longer durations of NIV. Furthermore, patients with underlying chronic respiratory failure might be discharged using long-term NIV (12).

INTERFACE SELECTION

The incidence of adverse effects, the type and intensity of adverse effects as well as the comfort depends on which type of interface is used and the duration of use. The major reason for intolerance to nasal masks is persistent air leakage through the mouth. Compared full face masks, nasal masks often have superior comfort and preserves speech and expectoration of secretions. The main reason for intolerance to a full face mask is related to discomfort such as dry mouth, sore eyes, claustrophobia and pressure site ulcerations. Air leaks are typically only a minor problem with full face masks compared to nasal masks (15, 16). Different mask sizes, shapes and models should be available to provide the best fit in each patient. An interface design which achieves an adequate air seal with a minimum degree of pressure to ensure a comfortable fit is of dominant importance to avoid interface-related adverse effects (13, 14). Due to complications such as discomfort, skin breakdown and air leaks during use of full face masks and nasal mask interfaces, alternative interfaces, such as the total face mask and the helmet, have been developed.

INTERFACES FOR NONINVASIVE VENTILATION

Potential Complications Related to Interfaces

Several types of interfaces are commercially available to connect the patient’s airway to the ventilator tubing for noninvasive ventilation application. The most commonly used interfaces include full face masks and nasal face masks such as the RespCare Utopia® and the RespCare Sylent®, respectively (Figure 1). A new and alternative interface is provided by the RespCare Hybrid® mask which is designed to avoid common problems such as nasal bridge injuries and claustrophobia, often arising during use of traditional face masks, (Figure 1). Although NIV is generally perceived as more comfortable for patients than invasive ventilation, interface intolerance remains a major cause of noninvasive ventilation failure. Interface-related adverse effects may account for up to 50-100% of all complications associated with NIV (13, 14). The problems include excessive air leaks, skin lesions at the site of skin-interface contact, claustrophobia, CO₂ re-breathing, facial pain and oronasal dryness. Excessive air leaks are a major challenge and results from a poor fit between the mask and the face. Excessive leaks may reduce alveolar ventilation and synchrony between the patient and the ventilator. Skin lesions at the site of mask contact are another common complication of noninvasive ventilation. Particularly the thin skin over the bony prominence at the nasal bridge is predisposed to pressure-induced skin breakdown (13, 14).

The helmet, consisting of a transparent hood and a soft collar has the unique feature of avoiding direct contact with the facial skin. However, despite encouraging results from nonrandomized clinical trials, there are concerns on the use of the helmet as opposed to conventional interfaces, in particular regarding the efficacy in decreasing inspiratory muscle effort and a poor patient-ventilator synchrony (17). Clinical studies using the total face mask for noninvasive ventilation have also shown promising results although oronasal dryness and claustrophobia was a more common patient complaint compared to traditional interfaces (14).

Interface Selection

The interface preference differs between acute and chronic respiratory failure. In acute respiratory failure, noninvasive ventilation using a full face mask (63%), is most common, followed by the use of a nasal mask (31%), nasal pillows and a mouth piece (16). A nasal mask requires that the patient keeps the mouth continuously closed which is often difficult in patients severely short of breath such as during acute respiratory failure (5). In clinical practice it is common to manage acute respiratory failure with continuous full face mask noninvasive ventilation and as the patient improves, intermittent use of noninvasive ventilation delivered through either a full face mask or a nasal mask is considered. In chronic respiratory failure, the common interface used is nasal mask (73%) followed by nasal pillows, full face masks and mouth pieces.
It is highly unlikely that any one mask will prove to be optimal for all NIV applications. Many publications on acute applications of NIV have used full face masks, largely because of the commonly held belief that patients with acute respiratory failure are “mouth breathers”. On the other hand, there is only limited evidence that the facial mask is more effective in the acute setting than nasal masks. The facial mask may be a reasonable first choice for acute applications of NIV but switching to a nasal mask should be considered if NIV is continued for more than a few days. Some patients, particularly those with claustrophobia, may prefer nasal masks over facial masks as a first choice for acute applications (13). By providing various types of interfaces, Ambu is able to support the user with interfaces for both acute and chronic respiratory failure. Ambu provides both a full face mask, the RespCare Utopia®, a nasal mask, the RespCare Sylen and nasal prongs (pediatric), the InnoMed Nasal Aire II Petite. In addition, Ambu provides the RespCare Hybrid® interface designed with a less claustrophobic design compared to traditional full face masks. The fact that the RespCare Hybrid® does not cover the nose also eliminates the risks for nasal bridge sores commonly reported from the use of traditional full face masks. All NIV interfaces provided by Ambu are designed to increase patient comfort and compliance. Dependent on the user’s preferences in various clinical settings, Ambu can provide a suitable interface for noninvasive ventilation therapy.

REFERENCES