Noninvasive Mechanical Ventilation in Patients with High-Risk Infections and Mass Casualties in Acute Respiratory Failure: Pediatric Perspective

29

Ozlem Teksam and Benan Bayrakci

Keywords

Noninvasive ventilation • Children • Acute respiratory failure • Pandemic • Influenza

---

29.1   Introduction

Respiratory problems are common symptoms in children and common reason for visits to the pediatric emergency department (PED) and admission to the pediatric intensive care unit (PICU). Although the great majority of cases are benign and self-limited, requiring no intervention, some patients need respiratory support. Invasive mechanical ventilation (IMV) is a critical intervention in many cases of acute respiratory failure (ARF), but there are absolute risks associated with endotracheal intubation (ETI). On the other hand, noninvasive ventilation (NIV) is an extremely valuable alternative to IMV. A major reason for the increasing use of NIV has been the desire to avoid the complications of IMV. It is generally much safer than IMV and has been shown to decrease resource utilization. Its use also avoids the complications and side effects associated with ETI, including upper airway trauma, laryngeal swelling, postextubation vocal cord dysfunction, nosocomial infections, and ventilator-associated pneumonia. There are a number of advantages

O. Teksam, MD
Division of Pediatric Emergency Medicine, Department of Pediatrics,
Hacettepe University Faculty of Medicine, Ankara, Turkey
e-mail: oteksam@yahoo.com

B. Bayrakci, MD (✉)
Division of Pediatric Intensive Care, Department of Pediatrics,
Hacettepe University Faculty of Medicine, Ihsan Dogramaci Children's Hospital,
Sihhiye, Ankara 06100, Turkey
e-mail: bbenan@yahoo.com

of NIV including leaving the upper airway intact, preserving the natural defense mechanisms of the upper airways, decreasing the need for sedation, maintaining the ability to talk while undergoing NIV, and reducing the length of hospitalization and its associated costs [1–3].

Noninvasive ventilation in the pediatric population with ARF as a therapeutic tool has become an option in recent years and is being applied increasingly. It can be initiated wherever the patient presents with ARF—in the PED, PICU, or other areas of the hospital. Over the last decade, several studies have suggested successful application of NIV in patients with ARF. Although numerous controlled studies and meta-analyses have shown its efficiency in different forms of ARF (e.g., exacerbation of chronic obstructive pulmonary disease and acute cardiogenic pulmonary edema in adults), the evidence supporting its using in infants and children with ARF is still limited, and there are no generally accepted guidelines for its use. However, the most recent physiological and randomized studies indicate that the early application of NIV improves the breathing pattern and gas exchange and reduces respiratory muscle effort in children [1–7].

Today, NIV is considered a first-line intervention for various causes of ARF and may be considered in the context of pandemics such as H1N1 or severe acute respiratory syndrome (SARS). In these circumstances, most of the studies showed that the use of NIV decreased the rate of ventilator-associated pneumonia and reduced the duration of oxygen requirement without prolonging the hospital stay [4–8]. On the other hand, there is controversy about the possibility that NIV increases the spread of viral infections during pandemics. Moreover, since the outbreak of SARS in 2003, pandemic planners around the world have classified NIV as a high risk procedure that should be used cautiously because of possible spread of the infection [9]. Similarly, Ontario's Provincial Infectious Diseases Advisory Committee in Canada recommended that NIV be avoided for patients with febrile respiratory illness during the 2009 influenza pandemic (H1N1) [10]. Additionally, the World Health Organization's interim guidelines on the prevention and control of acute respiratory diseases associated with health care have included NIV among the aerosol-generating procedures in which there is possibly an increased risk of respiratory pathogen transmission [11]. However, there has been no evidence-based information to support the claim that the use of NIV increases the risk of transmitting infectious diseases.

29.2   Analysis

The use of NIV for children with ARF caused by viral infections and experiences using NIV in these children are increasing worldwide. In the literature, most of the studies related to using NIV in the case of ARF have been done during pandemics. Also, there is still a large variety of practices and a paucity of published data in pediatrics. Nonetheless, after the most important two viral pandemics during the last decade, especially the last one with influenza A(H1N1), most of the societies

including above-mentioned and the European Respiratory Society, European Society of Intensive Care Medicine, and The American Association for Respiratory Care have recommended that NIV not be used to treat ARF due to H1N1, particularly in severely ill patients. Thus, NIV is accepted as a high-risk procedure that should be used cautiously because of possible spread of infection [9–15].

During the last decade, we experienced two viral pandemics that ultimately spread worldwide. One was occasioned by severe acute respiratory syndrome (SARS), which is an emerging infectious disease that first manifested in humans in China in 2002. In an observational study of the SARS outbreak that included adult patients from China, the effectiveness of NIV in the treatment of ARF was investigated. It was shown that NIV was effective in preventing the use of endotracheal intubation in 70 % of patients because of its early initiation in the SARS patients. In this study, none of the health workers, including doctors, nurses, and health-care assistants, acquired SARS from the patients. As an explanation, NIV was applied in a negative-pressure environment with strict personal protection and close monitoring of the health status of all involved staff [4]. In another study from Toronto during SARS, the use of NIV was discouraged especially after clinicians contracted the disease when a patient was intubated following NIV failure [9]. Therefore, some clinicians considered NIV contraindicated for ARF due to airborne respiratory diseases unless it is used in a negative-pressure isolation room and strict precautions are taken [4, 9].

The second viral pandemic was influenza A(H1N1) in 2009. The role of NIV in children with ARF due to influenza A(H1N1) was also the subject of controversy, although NIV has become an important mechanism for ventilator support for pediatric ARF. Severe respiratory failure is a well-recognized complication of pandemic H1N1 influenza infection. Rello et al. [16] applied NIV to a small number of critically ill patients with pandemic H1N1 infection complicated by ARF. Most of these patients subsequently required IMV support. Therefore, NIV is generally not recommended for patients with the novel influenza infection complicated by pneumonia and ARDS. NIV temporarily improves oxygenation and reduces the work of breathing but does not necessarily alter the course of the disease. The need for NIV is an indication of severe disease and likelihood of IMV. In addition, hemodynamic instability and multi-organ failure are contraindications for applying NIV [2, 16, 17].

In a multicenter study from India that included adult patients with infected influenza A(H1N1) during the outbreak of influenza A(H1N1) in 2009, patients requiring invasive ventilation at admission had a higher mortality rate than those managed with NIV and those not requiring ventilation. NIV was considered based on guidelines regarding ARF that included severe dyspnea at rest [respiration rate (RR) > 35/min], $PaO_2/FiO_2 < 200$ while breathing oxygen through a mask, and use of accessory muscles of respiration or paradoxical abdominal motion. Criteria for a response to NIV, or lack of it, were RR improvement, the Glasgow Coma Score (GCS), and blood gases improvement. Intubation was considered if there was intolerance to the mask or there was a contraindication to continued use, including nasal bridge

necrosis, persistent hypoxemia not responding to appropriate and tolerated levels of positive end-expiratory pressure (PEEP), or persistent or worsening respiratory acidosis. In all, 32.1 % of patients were managed with NIV. However 17 % of all patients failed NIV and were intubated and ventilated invasively. Patients who could be started on and managed with NIV had significantly better survival compared with those who required IMV at the onset. The need for invasive ventilation at admission was found to be associated with a higher mortality rate [18].

In another multicenter observational study, Nicolini et al. [19] showed that NIV was effective in preventing endotracheal intubation in 48 % of the patients with ARF and pulmonary infiltrates due to an H1N1 infection. Moreover, NIV success was found to be associated with a lower incidence of "new" infectious complications and increased ICU survival compared to those patients who failed NIV. Additionally, a high Simplified Acute Physiology Score (SAPS II) and a low PaO_2/FiO_2 are related to high risk of intubation and mortality. Therefore, they emphasized that the timing of NIV application is crucial in determining its success [19].

In a multi-center study investigating the outcome of critically ill children with H1N1 in PICUs from Turkey, NIV was applied 7.2 % of all patients. Two of them survived (3.4 %) and four did not (16.0 %). In the same study, mortality rates were found to be higher in patients with H1N1 infection and conventional mechanical ventilation. However, multi-organ failure and high mortality and organ dysfunction scores were associated with increased mortality. The nonsurvivor group required conventional mechanical ventilation, high-frequency oscillatory ventilation, renal replacement therapies, inotropes, and vasoactive treatment. However, this study is not enough to discuss NIV efficiency because NIV was applied in a small number of patients and high mortality rates were found [20].

Torres et al. [7] described the clinical characteristics and outcome of children admitted to the PICU with influenza A(H1N1) from Argentina during the 2009 pandemic. NIV was applied to 13.3 % of all patients (19/142) and the success rate was 63 % with no deaths. Twelve of these patients recovered from NIV without mechanical ventilation. Although there was a high rate of mortality (47 %) in their study, all of the children who received NIV survived. Age < 24 months, mechanical ventilation, use of inotropes, respiratory co-infections, and a history of asthma were found as predictors of mortality [7]. The use of NIV versus conventional ventilation was addressed in another randomized trial that included a selected small group of hypoxemic patients. According to the results, serious infections secondary to intubation developed more frequently in the conventional ventilation group. The duration of ventilation and the ICU stay were shorter in the NIV group [1].

Another controversial aspect of NIV application is whether NIV should be used in patients with acute respiratory distress syndrome (ARDS) due to pneumonia or other causes. According to a consensus in Spain, NIV cannot be considered a technique of choice in adult patients with ARDS, although it may be useful in experienced centers and in cases of ARF. Within this consensus, the failure rate of NIV in

patients with ARF secondary to ARDS due to influenza virus A(H1N1) infection was 75 %, the mortality rate among the patients in which NIV failed was 38 %, and delays in starting intubation were associated to an increase mortality risk. The general recommendation was that early intubation of patients with evidence of NIV failure should be instituted for better results [21].

There is also controversy about the use of NIV in children with ARDS. There are only two studies in children with ARDS, and they encourage the use of NIV. Essouri et al. [6], in a descriptive study, recommended that NIV be used as the first line intervention in children with severe ARF due to community-acquired pneumonia or respiratory failure in immunocompromised patients, although the failure rate in their study was 78 % among patients with ARDS. Munoz-Bonet et al. [5] reported an NIV success rate of 81 % regarding control of ARF due to pneumonia, thereby avoiding tracheal intubation and its complications. Two parameters were associated with NIV failure, including MAP > 11.5 cmH$_2$O and the FiO$_2$ (0.6). On the other hand, the NIV success rate was 50 % in patients with ARDS. Therefore, the authors thought that the diagnosis of ARDS should not be a contraindication for the use of NIV, especially in immunosuppressed patients because it prevents tracheal intubation They also recommended that NIV be applied as early as possible.

Fowler et al. [22] investigated the risk of contracting SARS among physicians and nurses who cared for patients with SARS during the epidemic. They showed that the nurses and physicians who directly participated in endotracheal intubation had a dramatically increased risk of developing SARS. Similarly, nurses caring for patients undergoing NIV may have been more likely to develop SARS than nurses caring for patients with SARS treated with conventional ventilation. The difference, however, was not statistically significant. Their study indicated that tracheal suctioning was one of the certain high-risk components of SARS nursing care, but it was not generally performed in patients with SARS ventilated with NIV. Therefore, endotracheal suction might be considered not to increase the risk of respiratory droplet dispersion.

During the SARS outbreak, SARS working groups developed guidelines for procedures, including endotracheal intubation, cardiopulmonary resuscitation, and mechanical ventilation. These guidelines specify that the use of personal protection devices is mandatory, the most qualified individual available should perform the endotracheal intubation, and procedures such as prolonged NIV and aerosolized bronchodilator or humidification therapies generally should not be initiated where safe alternatives are available. At that time, many clinicians seeing patients during the Asian SARS outbreak thought that NIV was preferred over early endotracheal intubation and mechanical ventilation because of the risk to HCWs involved with endotracheal intubation [21–24].

Influenza viruses are thought to be spread by droplets, but the role of aerosol dissemination is unclear. Droplets in the respirable range (~5 μm) may play a significant part in transmission, but the role of aerosols has been questioned.

There are few studies that have quantified the viral load in droplets or aerosols. A subgroup of patients, often with underlying chronic disorders or risk factors such as immunosuppression, can develop pneumonia/respiratory insufficiency with H1N1 swine flu or other influenzal infection and require treatment by oxygen therapy, nebulized medication, and ventilatory support. These therapies are thought to generate droplets or aerosols. Based on pandemic experience, gas leakage via exhalation ports may also disperse infectious particles into the environment. During pandemics, HCWs and other patients are at risk for contamination because of the virus. In addition, pandemic planners have highlighted the potential need for providing mechanical ventilation in environments that are safe for HCWs. They have recommended airborne precautions for HCWs who are managing patients with pandemic influenza with increased transmissibility and during procedures that may generate small aerosol particles of respiratory secretions. However, it is not known how exhaled air and particles may disperse during NIV in clinical settings. There is no reliable marker that can be safely introduced to the patients [23–25].

Previous studies have not assessed droplet or aerosol generation during respiratory support interventions in clinical practice. Hui et al. [24] assessed the risks of single-circuit NIV in spreading infectious particles through the bleeding port and orofacial mask interface using a high-fidelity human patient simulator. They showed that substantial exposure to exhaled air occurred within 0.5 m from patients receiving NIV, and higher ventilator pressures result in a wider distribution of exhaled air (Fig. 29.1). Therefore, they recommended that HCWs be aware of the potential risks of viral transmission during NIV and take strict contact and droplet precautions, wearing full personal protective equipment.

An observational study of influenza A and influenza B in exhaled breath also showed viral RNA in one-third of infected patients, and 99 % of particles had a diameter of <5 µm when sampled during tidal breathing [25]. Generally, NIV and chest physiotherapy are accepted as droplet-generating procedures, producing droplets of >10 µm. Because of their large mass, most fall on local surfaces within 1 m. Therefore, HCWs providing NIV and chest physiotherapy working within 1 m of an infected patient should have a higher level of respiratory protection. Infection control measures designed to limit aerosol spread, such as negative-pressure rooms, may have less relevance. The results of these studies may have infection control implications for other airborne infections, such as SARS and tuberculosis, as well as for pandemic influenza infection [10, 22, 25].

Simonds et al. [23] showed the characteristics of droplet/aerosol dispersion around delivery systems during NIV treatment by measuring droplet size, geographical distribution of droplets over time after the interventions were discontinued, and the impact of modification of the NIV circuit in clinical practice. They found that NIV using a vented mask produced large droplets (>10 µm) from patients and coryzal subjects compared with baseline values. This increase in large droplets was not seen using the NIV circuit modification. Preliminary analysis suggests that droplet size falls to within a baseline range within 20–40 min of discontinuing NIV [23].
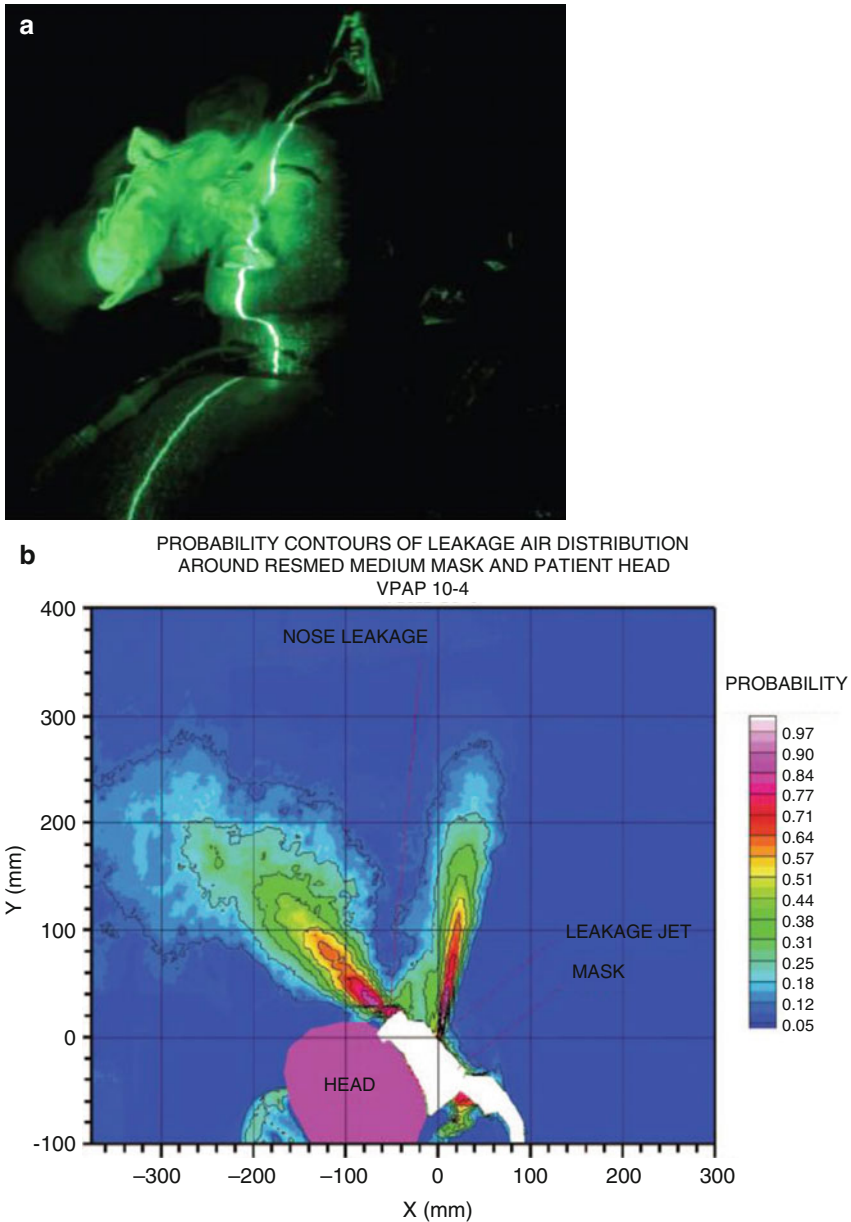
Fig. 29.1 (**a**) Airflow leakage around a mask is shown by a laser light sheet. Visualization of airflow around the oronasal mask was facilitated by marking the air with smoke particles produced by an M-6000 smoke generator (model N19; DS Electronics, Tempe, AZ). The laser light sheet illuminated the smoke particles after the mask airflow leakage. (**b**) Inspiratory/expiratory positive airway pressures (IPAP 10 cmH₂O/EPAP 4 cmH₂O) with leakage from the nasal bridge (sagittal plane). There is a <10 % probability of exposure if the health care worker (HCW) stands outside the light blue contour regions. If the HCW is standing outside a radial distance of approximately 0.25 m from the mask, there is <10 % chance of exposure to the exhaled air. (**c**) Note that the highest probability of encountering the patient's exhaled air is not directly above the mask in the sagittal plane but to the side, where a HCW may typically stand (From Hui et al. [24])
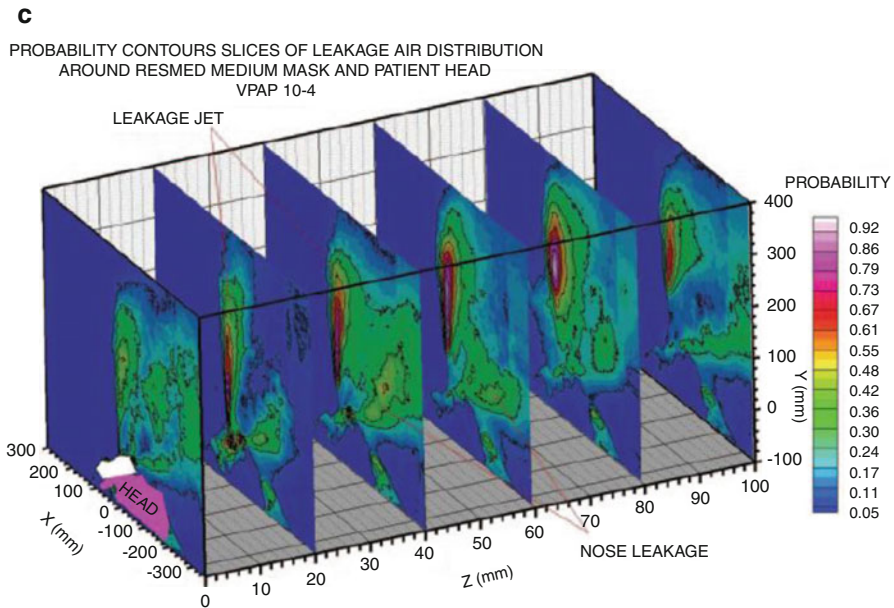
c

PROBABILITY CONTOURS SLICES OF LEAKAGE AIR DISTRIBUTION
AROUND RESMED MEDIUM MASK AND PATIENT HEAD
VPAP 10-4

Fig. 29.1 (continued)

29.3   Discussion

Noninvasive ventilation is an effective treatment modality for patients with ARF due to pneumonia or acute cardiogenic pulmonary edema and for immunocompromised patients, both adults and children, with pneumonia and postextubation respiratory failure. It is also known that NIV can markedly reduce the need for endotracheal intubation and the rate of complications. It shortens the hospital length of stay and improves survival. NIV can be used to decrease a patient's dyspnea and work of breathing and improve gas exchange. Therefore, patients with hypercapnic forms of ARF are most likely to benefit from NIV. However, clinicians should not forget that NIV is a complementary technique and cannot replace endotracheal intubation under all conditions.

The success of NIV relies on several factors, including the type and severity of ARF, very low arterial blood pH, marked alteration in mental status, underlying disease, location of treatment, and the experience of the team. The time factor is also important. To prevent further deterioration, early NIV must become an important part of the first-line treatment of ARF. In addition, the success of invasive ventilation is dependent on various clinical aspects and the organisation of care—but also on a number of technical issues. These technical points are the ventilator interface, type of humidifier, and ventilator used and its capabilities for triggering and pressurization. The general care of the NIV patient is different from that for a patient

undergoing invasive ventilation and potentially has a great influence on the success of the technique.

Noninvasive ventilation has become an important mechanism for ventilator support in children with ARF. However, if the ARF is due to the influenza A(H1N1) virus, NIV has become controversial. Future prospective randomized controlled studies should help determine, with more methodology, the physiological effects of NIV and the most appropriate group of patients potentially able to benefit from this promising technique during a pandemic. The studies have shown that in critically ill children with confirmed or probable H1N1 viral infection and severe ARDS the use of NIV can result in significant improvement in oxygenation. It may improve the mortality rate for this very high-risk population.

We believe that NIV is a promising alternate to standard therapies in the treatment of ARF in pediatric patients. In our experience, patients placed on NIV should be monitored closely and the mode of ventilation reviewed if there is a lack of response within a few hours after starting therapy. Treatment of early ARDS associated with respiratory viral infections—e.g., influenza A(H1N1)—using NIV could also be tried after identifying patients who require endotracheal intubation in negative-pressure rooms under strict precautions. Because of the high demand for critical care beds during a pandemic, NIV may have a role in reducing the estimated ICU load as it can be applied anywhere in the hospital.

In conclusion, the efficiency of NIV in children with ARF depends on the degree of hypoxia, the underlying disease, and illness severity scores. NIV can even be used in immunosuppressed patients, although cautiously, because intubation is a strong predictor of mortality and nosocomial infections. The success rate of NIV depends on early application, the experience of the institution, and the team's familiarity with the technique.

Key Major Recommendations
- Noninvasive ventilation can be regarded as an option of choice in children with ARF and ARDS due to respiratory viral infections in centers with a large experience and under conditions of strict personal protection.
- Initiating procedures that may be associated with increased dispersal of respiratory droplets—as in patients with SARS or influenza A(H1N1)—must be conducted with caution. There may be risks that require many forms of support. Decisions must be made on an individual patient basis with due attention to the hazards for both patients and HCWs.
- The outcome of NIV in patients with ARF due to acute lung injury, ARDS, or pneumonia depends on the degree of hypoxia, the presence of co-morbidities and complications, and the illness severity score. In these circumstances, NIV should be cautiously considered early and not delay needed intubation.

References

1. Antonelli M, Conti G, Rocco M, Bufi M, et al. A comparison of noninvasive positive-pressure ventilation and conventional mechanical ventilation in patients with acute respiratory failure. N Engl J Med. 1998;339:429–35.
2. Nava S, Ceriana P. Causes of failure of noninvasive mechanical ventilation. Respir Care. 2004;49:295–303.
3. Calderini E, Chidini G, Pelosi P. What are the current indications for noninvasive ventilation. Curr Opin Anaesthesiol. 2010;23:368–74.
4. Cheung TMT, Yam LYC, Lau ACW, Kong BMH, Yung RWH. Effectiveness of noninvasive positive pressure ventilation in the treatment of acute respiratory failure in severe acute respiratory syndrome. Chest. 2004;126:845–50.
5. Munoz-Bonet JI, Flor-Macian EM, Brines J, Rosello-Millet PM, et al. Predictive factors for the outcome of noninvasive ventilation in pediatric acute respiratory failure. Pediatr Crit Care Med. 2010;11:675–80.
6. Essouri S, Chevret L, Durand P, Haas V, et al. Noninvasive positive pressure ventilation: five years of experience in a pediatric intensive care unit. Pediatr Crit Care Med. 2006;7:329–34.
7. Torres SF, Lollster T, Schnitzler J, Farias JA, et al. High mortality in patients with influenza A pH1N1 2009 admitted to a pediatric intensive care unit: a predictive model of mortality. Pediatr Crit Care Med. 2012;13:e78–83.
8. Javouhey E, Barats A, Rishard N, Stamm D, Floret D. Noninvasive ventilation as primary ventilatory support for infants with severe bronchiolitis. Intensive Care Med. 2008;34:1608–14.
9. Poutanen SM, Low DE, Henry B, Finkelstein S, et al. Identification of severe acute respiratory syndrome in Canada. N Engl J Med. 2003;348:1195–2005.
10. Provincial Infectious Diseases Advisory Committee (PIDAC). Preventing febrile respiratory illnesses. Ottawa: Ontario Ministry of Health and Long Term Care; 2006. Available: www.health.gov.on.ca/english/providers/program/infectious/diseases/best_prac/bp_fri_080406.pdf. Accessed 27 July 2009.
11. World Health Organization. Infection and control of epidemic-and pandemic-prone acute respiratory diseases in health care. WHO interim guidelines. World Health Organization; 2007. http://www.who.int/csr/resources/publications/WHO_CD_EPR_2007_6/en/. Accessed 19 Mar 2009.
12. Nava S, Schreiber A, Domenighetti G. Noninvasive ventilation for patients with acute lung injury or acute respiratory distress syndrome. Respir Care. 2011;56:1583–8.
13. Conti G, Larrsson A, Nava S, Navalesi O. On the role of noninvasive (NIV) to treat patients during the H1N1 influenza pandemic. http://dev.ersnet.org/uploads/Document/63/WEB_CHEMIN_5410_1258624143.pdf
14. Nin N, Soto L, Hurdato J, Lorente JA, et al. Clinical characteristics and outcomes of patients with 2009 influenza A(H1N1) virus infection with respiratory failure requiring mechanical ventilation. J Crit Care. 2011;26:186–92.
15. McCracken J. The consequences of withholding noninvasive ventilation during an epidemic (letter). Respir Care. 2009;54:1412–3.
16. Rello J, Rodriguez A, Ibanez P, Socies L, et al. H1N1 SEMICYUC Working Group. Intensive care adult patients with severe respiratory failure caused by influenza A (H1N1) in Spain. Crit Care. 2009;13:R148.
17. Hui DS, Lee N, Chan PKS. Clinical management of pandemic 2009 Influenza A (H1N1) Infection. Chest. 2010;137:916–23.
18. Ramakrishna K, Sampath S, Chacko J, Chacko B, et al. Clinical profile and predictors of mortality of severe pandemic (H1N1) 2009 virus infection needing intensive care: a multi-centre prospective study from South India. J Glob Infect Dis. 2012;4:145–52.
19. Nicolini A, Tonveronachi E, Navalesi P, Antonelli M, et al. Effectiveness and predictors of success of noninvasive ventilation during H1N1 pandemics: a multicenter study. Minerva Anestesiol. 2012;78:1333–40.

20. Kendirli T, Demirkol D, Yıldızdaş D, Anıl AB, et al. Critically ill children with pandemic influenza (H1N1) in pediatric intensive care units in Turkey. Pediatr Crit Care Med. 2012;13:e11–7.
21. Rodriguez A, Alvarez-Rocha L, Sirvent JM, Zaragoza R, et al. Recommendations of the infectious diseases work group (GTEI) of the Spanish Society of Intensive and Critical Care Medicine and Coronary Units (SEMICYUC) and the infections in critically ill patients study group (GEIPC) of the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC) for the diagnosis and treatment of influenza A/H1N1 in seriously ill adults admitted to the intensive care unit. Med Intensiva. 2012;36:103–37.
22. Fowler RA, Guest CB, Lapinsky SE, Sibbald WJ, et al. Transmission of severe acute respiratory syndrome during intubation and mechanical ventilation. Am J Respir Crit Care Med. 2004;169:1198–202.
23. Simonds AK, Hanak A, Chatwin M, Morrell MJ, et al. Evaluation of droplet dispersion during noninvasive ventilation, oxygen therapy, nebuliser treatment and chest physiotherapy in clinical practice: implications for management of pandemic influenza and other airborne infections. Health Technol Assess. 2010;14:131–72.
24. Hui DS, Hall SD, Chan MTV, Chow BK, et al. Noninvasive positive-pressure ventilation: an experimental model to assess air and particle dispersion. Chest. 2006;130:730–40.
25. Fabian P, McDevitt JJ, DeHaan WH, Fung ROP, et al. Influenza virus in human exhaled breath: an observational study. PLoS One. 2008;3:e2691.