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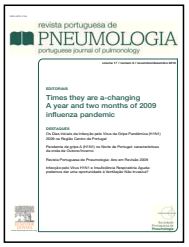

ARTIGO DE REVISÃO

H1N1 infection and acute respiratory failure: can we give non-invasive ventilation a chance?

João Carlos Winck* and Miguel Gonçalves

Faculdade de Medicina da Universidade do Porto, Porto-Portugal

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KEYWORDS
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Abstract
In 2009, a novel H1N1 Influenza virus has emerged and on June 11 the World Health Organization declared it as pandemic. It may cause acute respiratory failure ranging from severe Acute Respiratory Distress Syndrome to exacerbations of airflow limitation. Non-invasive ventilation is now considered first-line intervention for different causes of acute respiratory failure and may be considered in the context of H1N1 pandemic. Although infection control issues have been arisen, non-invasive ventilation was effective and safe during the Severe Acute Respiratory Syndrome in Asia. It is reasonable to recommend non-invasive ventilation in H1N1-related exacerbations of chronic respiratory diseases, especially in negative-pressure wards. Treatment of early Acute Respiratory Distress Syndrome associated with H1N1 using non-invasive ventilation could be tried rapidly identifying those who fail without delaying endotracheal intubation. Considering the high demand for critical care beds during the pandemic, non-invasive ventilation may have a role in reducing the estimated load.

PALAVRAS-CHAVE
Acute respiratory failure;
H1N1 Influenza virus;
Non-invasive ventilation

Infecção pelo H1N1 e insuficiência respiratória aguda: será que podemos dar a ventilação não-invasiva uma oportunidade?

Resumo
Em 2009, surgiu um novo vírus da gripe H1N1 e a 11 de Junho a Organização Mundial de Saúde declarou-o como uma pandemia. Poderá causar insuficiência respiratória, do Síndroma de Dificuldade Respiratória Agudo a manifestações de limitação do fluxo de ar. A ventilação não invasiva é agora considerada como a primeira intervenção para diferentes causas de insuficiência respiratória aguda e pode ser considerada no contexto da pandemia de H1N1. Apesar de terem

*Corresponding author.
E-mail: jwinck@hsjoao.min-saude.pt (J.C. Winck).

surgido problemas ligados ao controlo da infecção, a ventilação não invasiva foi eficaz e segura durante o Síndroma de Dificuldade Respiratória Agudo na Ásia. É razoável recomendar a ventilação não invasiva nas manifestações de doenças respiratórias crónicas ligadas ao H1N1, especialmente em serviços com pressão negativa. O tratamento do Síndroma de Dificuldade Respiratória Agudo precoce associado ao H1N1 utilizando ventilação não invasiva pode ser experimentado para identificar rapidamente aqueles que falham sem atrasar a intubação endotraqueal. Considerando a elevada procura de camas de cuidados intensivos, a ventilação não invasiva pode ajudar a reduzir a sobrelotação estimada.

Introduction

In April 2009 a new strain of human H1N1 influenza A virus was identified in California.[1] As of November 15 it has caused 526,060 cases worldwide and at least 6,770 deaths in more than 206 countries.[2]

Influenza is normally a self-limited acute respiratory infection. However, the recent circulation of influenza A (H1N1) virus has been associated with severe disease and with excess pneumonia.[3] Data from Australia's winter revealed a hospitalization rate of 23 per 100,000 population with 13% of ICU admission.[4] The Canadian prospective study of critically ill patients with 2009 influenza (H1N1) infection revealed that major co-morbidities were present in only 30,4% of patients and was associated with severe hypoxemic respiratory failure.[5]

Recent series from the US and Australia including critically ill patients with novel influenza A (H1N1) virus infection describe development of ARDS in 35.8% and 48.8% of cases and a 45% and 14.3% hospital mortality, respectively.[6,7] Exacerbation of chronic diseases (Chronic Obstructive Pulmonary Disease-COPD- and chronic heart failure) occurs in 14.9% of patients with H1N1 admitted to ICU in Utah[8] and exacerbation of airflow limitation in 13.9% of patients admitted to ICU in Australia and New Zealand.[7]

The role of non-invasive ventilation in Acute Respiratory Failure

Since its initial reports in the late 1980s NIV has become a first-line intervention for different causes of acute respiratory failure (ARF).[9] It reduces intubation rate and mortality in ARF due to exacerbations of COPD[10] and acute cardiogenic pulmonary oedema.[11] However, data from surveys across the world suggests that NIV is still underused in some centres.[12]

The role of NIV for hypoxemic respiratory failure is more controversial. However, it has been demonstrated in a randomized controlled trial that, with similar settings, NIV is equivalent to conventional ventilation in improving gas exchange with lower incidence of ventilator associated pneumonia.[13] According to a a large multicentric study, only 31% of ARDS patients are eligible for NIV, but this intervention avoided intubation in around 50% of cases;[14] those with Simplified Acute Physiology Score ≤ 34 and $PaO_2/FIO_2 > 175$ after one hour were more likely to benefit from NIV.

Non-invasive ventilation: the experience gained from Severe Acute Respiratory Syndrome

Severe Acute Respiratory Syndrome (SARS), due to a novel coronavirus, emerged in 2002, with significant morbidity and mortality. Critically ill patients with SARS presented with Acute Lung Injury/ARDS in 82% of cases, with mortality at 28 days of 45%.[15] Those patients were at high risk of infecting health care workers (HCW), especially due to high-risk procedures coinciding with viral shedding peak.[16] Avoidance of non-invasive ventilation (NIV) and other aerosol-generating procedures were recommended in Canadian guidelines to minimise the occupational risk and nosocomial transmission.[17] However, this was due to a non-significant increased risk from a retrospective ICU cohort analysis and others recommended NIV for respiratory distress and refractory hypoxemia in newly designed SARS wards.[18] In fact, NIV has been reported to be effective in SARS-related Acute Respiratory Failure without posing infection risks to HCW.[19] Yam LYC et al suggest that compared to invasive ventilation, NIV for ARF in SARS was associated with reduced mortality without any NIV-related SARS transmission within the 21 patients treated.[19] Moreover Cheung et al[20] in a retrospective analysis of 20 patients state that NIV (also performed in negative pressure rooms) avoided intubation in 70% of cases and none of the 105 HCW caring for the patients acquired SARS. Another series in China reported the experience with NIV in 28 patients with SARS showing physiologic improvement and avoiding intubation in 67% and none of the HCW contracted SARS.[21] In the US another report confirms the lack of SARS transmission among 110 HCW with exposure to 6 SARS patients.[22]

Non-invasive ventilation in H1N1 infection: the debate

Recently there has been some debate in literature about the use of NIV in the context of H1N1.[23] Should it be considered a high-risk procedure? Is it an effective ventilatory support in this scenario?

The concern of infectious droplet dispersion has been addressed by experimental models showing that exposure can occur within one metre of patients receiving Non-invasive Positive Pressure Ventilation.[24] However, it is questionable that a mannequin can confidently simulate NIV in real patients. Moreover wearing a face mask for NIV

Table 1 Use of NIV in H1N1 2009 major critically-ill series

Author	*Kumar A*	*Jain S*	*Ugarte S*	*Webb SA*	*Dominguez-Cherit G*	*Estenssoro E*
Reference	*5*	*6*	*28*	*7*	*26*	*27*
N	168	67	75	722	58	337
Country	Canada	US	Chile	Australia/NZ	Mexico	Argentina
NIV use (N / %)	55(32.7%)	NR	4(7%)	NR	6 (10%)	64 (19%)
NIV success (N / %)	8(14.6%)		4(100%)		?	3 (5%)

N-number of cases; % Percentage.

can protect against particle generation during coughing and sneezing.

Due to the efficacy previously described in SARS, NIV can be an attractive option especially in a pandemic scenario when the demand for critical care may be massive.[25]

Non-invasive ventilation in H1N1 infection: the ongoing experience

Among the recently published major series of critically ill patients with novel influenza A (H1N1) virus infection,[5-8,26-28] NIV has been reported in four of them,[5,26-28] including 129 patients with a success ranging from 5% to 100% (table 1). Two smaller series[8,29] (in which NIV was tried in 21 patients) (table 2) and six case series (including 10 patients)[30-35] describe success in 6 cases (20%).

The majority were patients with severe ARDS in whom ventilatory support ranged from CPAP[33] to bi-level ventilation.[30] No mention of ventilatory parameters[27-29,31,32] precludes some critical review of the negative results, but in the Spanish series Rello et al.[29] suggest that the Sequential Organ Failure Assessment score was higher in NIV failure. Moreover Estenssoro et al.[27] suggest that patients that used NIV were associated with a better outcome.

The impact of H1N1 infection on the southern hemisphere provided important lessons in critical care demand, revealing that in the epidemic peak in Australia and New Zealand the percentage of beds occupied by patients with H1N1 reached up to a maximum of 19%.[7]

In case ICU facilities cannot be expanded, NIV can be delivered in respiratory intermediate care units (RICU), offloading ICU beds. In fact during the H1N1 outbreak 4 Mexican patients died while awaiting ICU beds.[26]

From that previously described, approximately one-third of critically ill patients may be eligible for NIV. Moving from ventilatory support in the ICU to NIV in RICU may be crucial during H1N1 pandemic!

Novel influenza A (H1N1) virus infection among HCW: is there a cause for concern with non-invasive ventilation?

Nosocomial non-pandemic influenza outbreaks are usually underdetected and underreported but their consequences for hospitals in terms of morbidity and costs are considerable.[36]

Soon after the identification of novel influenza A (H1N1) virus infections in the US, 26 cases of infected HCW were reported by the CDC, 50% of which were deemed to have acquired it in the health-care setting.[37] Although no mention of aerosol-generating procedures that put HCW at risk is made, the report highlighted the need to implement infection-control strategies to prevent transmission of novel H1N1 in hospitals. Of the 13 HCWs who were infected, only three had consistently used personal protective equipment.[37]

Table 2 Use of NIV in H1N1 2009 smaller critically-ill series

Author	*Miller RR*	*Rello J*
Reference	*8*	*29*
N	47	32
Country	US	Spain
NIV use (N / %)	13 (in 30 ARDS)	8 (33%)
NIV success (N / %)	2 (15%)	2 (25%)

N-number of cases; % Percentage.

Concerning the case of HCW transmission, in the recent series of critically ill H1N1 patients this has been stated only in 4,[3,5,26,29] ranging from zero in the Canadian series[5] to 12% in the Mexican study.[3] To be highlighted is the fact that in the latter report the authors verified that no HCW were hospitalized after strict infection control measures were undertaken.[3] Since NIV is suggested as a risk factor for infection in hospital workers in these papers, although in some of the series there is omission of this information, it seems that the risk may not be so significant after all!

Published recommendations for the use of non-invasive ventilation during H1N1 pandemic

Recently the European Respiratory Society and the European Society of Intensive Care Medicine released some guidelines on the use and limitations of NIV in patients with confirmed H1N1 infection.[38] They suggest that NIV may be considered only in patients with mild to moderate hypercapnic acute respiratory failure, acute respiratory failure and/or distress due to cardiogenic pulmonary oedema, in the absence of pneumonia, multiple organ failure, and refractory hypoxemia.

The Australasian Society for Infectious Diseases (ASID) in a recent position statement also recommends that patients who require non-invasive ventilation should have priority for negative-pressure rooms if available.[39] This

has also been suggested by the UK Department of Health, which recommends use of a non-vented mask or helmet for NIV, a high-efficiency bacterial/viral filter between the non-vented mask and the expiratory port and at the outlet of the ventilator.[40] In another NHS document developed in conjunction with the British Thoracic Society and the Intensive Care Society it is advised that NIV should be provided with strict safety measure for the HCW and by experienced teams.[41] It is proposed that NIV can have a role in influenza-related pneumonia as an early intervention, particularly in those with co-morbidities such as COPD. Moreover it can constitute ceiling to ventilator care in patients with COPD or heart failure with DNI orders.

From the previous discussion and current literature it is clear that if certain recommendations are followed NIV can be effective and safe in the context of H1N1 infection. Hence, we propose that we should give NIV a chance and suggest the management principles depicted in the table 3.

Conclusion

While the pandemic is still evolving across the globe we are deeply convinced that non-invasive ventilation can have a role in treating acute respiratory failure patients, reducing the need of ICU beds and improving outcomes.

Although there are some authors that reject NIV in infectious patients[43] the experience from recent series suggests that clinicians are using it even in countries where guidelines suggest its avoidance.[5] It is reasonable to recommend NIV in Chronic Heart Failure[35] and COPD with exacerbations attributable to H1N1, given the strong evidence of NIV in non-H1N1 patients with similar diseases.[10,11] For those patients with H1N1 associated ARDS a thorough selection is needed, although some may respond to NIV.[30] In this context NIV should be applied with specific resources by experienced teams.

To strengthen the position on non-invasive ventilation in the ongoing H1N1 pandemic influenza we encourage all clinicians to report their experience with this technique in this setting. Active surveillance of nosocomial infections is also highly recommended.

Early diagnosis and therapeutic interventions for severe H1N1 pandemic influenza should also be emphasized.

Table 3 Management principles of NIV in H1N1 infection

Perform NIV preferably in negative pressure-rooms with remote monitoring
Health care workers should have personal protective equipment
Use a non-vented mask or helmet
Use viral filters in the circuit
Use ventilators with integrated FiO_2 control
In exacerbations of COPD, a pH < 7.25, APACHE II score ≥ 29, respiratory rate ≥ 30/min is associated with higher risk of NIV failure[42]
In hypoxemic patients initiate NIV when respiratory rate < 30/min or PaO_2/FiO_2 > 200 and < 300; exclude patients with SAPS score > 34[14]
Always consider a 2-hour window of opportunity. If physiological/clinical deterioration occurs proceed to intubation (in COPD a pH < 7.25 after 2 h greatly increases the risk of NIV failure[42]; in ARDS a PaO_2/FiO_2 ≤ 175 after 1 hour was also associated with NIV failure[14])

NIV-non-invasive ventilation; COPD-Chronic Obstructive Pulmonary Disease; APACHE-Acute Physiology and Chronic Health Evaluation; SAPS-Simplified Acute Physiology Score; ARDS-Acute Respiratory Distress Syndrome.

Conflict of interest

Authors declare they don't have any conflict of interest.

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