

the epidemic season, RSV may be isolated from respiratory samples of asymptomatic individuals; this carriage would be responsible for the transmission and spread of the infection, giving rise to seasonal outbreaks in the winter.<sup>1,3</sup>

In cases of bronchiolitis, it is difficult to establish which of the 2 viruses could be involved, although Reina et al.<sup>6</sup> reported that in the 1999–2000 period, 52.9% of bronchiolitis cases in the winter season were caused by influenza A virus (H3N2), without detection of RSV.

Thus, it appears that the incidence of coinfection by influenza viruses and RSV is very low, while it is difficult to infer the direct role of each virus in the pathogenesis of ARTIs in infants aged less than 1 year.

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## Non-invasive ventilation in acute bronchiolitis on the ward. A viable option<sup>☆</sup>

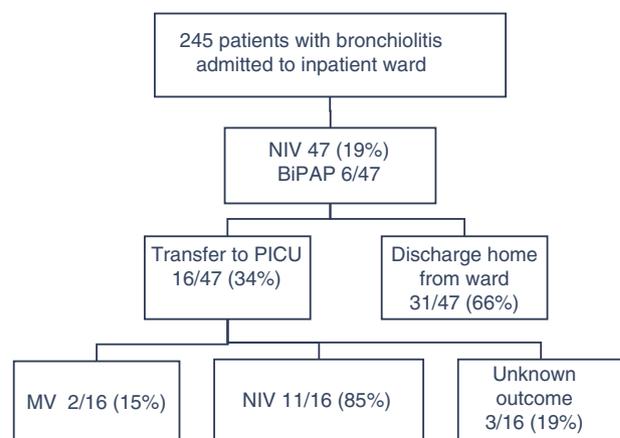


### Ventilación no invasiva en bronquiolitis aguda en la planta. Una opción viable

Dear Editor:

In developed countries, acute bronchiolitis (AB) is the most frequent reason for hospital admission in infants aged less than 1 year. Between 3% and 11% of the infants hospitalised with AB are transferred to the paediatric intensive care unit (PICU). The management of AB is based on supportive care, and in patients with moderate-to-severe AB, non-invasive ventilation (NIV) has become the first choice of respiratory support.<sup>1</sup> This is a technique whose use is generally restricted to PICUs, which, due to the seasonal pattern of AB, get overwhelmed during incidence peaks. Due to the need to find alternative solutions during the epidemic season, we started to use NIV in patients with moderate AB at the ward level, with the option to transfer them to a PICU if necessary, an approach that was already being practised in some European hospitals.<sup>2,3</sup> In this article, we describe our experience with this strategy and the observed clinical outcomes.

We conducted the study in a secondary care level hospital in the Community of Madrid. Of a total of 245 infants aged less than 6 months admitted with a diagnosis of AB between January 2013 and March 31 of 2017, 47 (19%) received NIV (Fig. 1). Our hospital does not have a PICU, and the nearest PICU is 15 min away by ambulance. We set up an area in the paediatric ward that included 2 beds (of the total of 18 available) that could be seen fully through a glass panel and



**Figure 1** Summary of patients admitted with AB that received NIV.

BiPAP, bilevel positive airway pressure; IMV, invasive mechanical ventilation; NIV, non-invasive mechanical ventilation; PICU, paediatric intensive care unit.

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accessed quickly, equipped for comprehensive monitoring (heart rate, respiratory rate, oxygen saturation [SatO<sub>2</sub>]) and with air and oxygen outlets and the necessary equipment for intubation and invasive mechanical ventilation (IMV). The nursing staffing in the ward was as follows: 3 nurses/2 nurse assistants in the morning and evening shifts, and 2 nurses/1 nurse assistant in the night shift. Staffing was not increased for the purpose of the study. After a period of 6 months during which the protocol was developed and all doctors, nurses and aides were trained in it, we introduced the use of NIV in patients with AB in January 2013. Patients with hypoxaemia (SatO<sub>2</sub> <90% with the ambient oxygen concentration) and mild respiratory distress (Respiratory Distress Assessment Instrument [RDAI] ≤5 or the Wood-Downes score modified by Ferres [mWDS] ≤3, depending on the physician in charge) received high-flow oxygen therapy (HFOT). The term *non-invasive ventilation* includes nCPAP (nasal continuous positive airway pressure) with a single level of air pressure and BiPAP (bilevel positive airway pressure) with two level pressures. The use of NIV was indicated in infants aged less than 3 months (limit imposed by the available material resources) with a diagnosis of AB presenting with hypercapnia (capillary PCO<sub>2</sub> ≥ 60 mmHg) and/or apnoea and/or moderate to severe respiratory distress (RDAI, 6–7; mWDS, 4–7). We excluded patients with underlying respiratory disease or altered level of consciousness. **Table 1** summarises epidemiological and respiratory data. All patients tolerated NIV well, and none developed complications.

In the management of moderate to severe AB, respiratory support starts with administration of HFOT with warmed and humidified oxygen and can be escalated to NIV and then IMV. It is believed that both NIV and HFOT can improve work of breathing and oxygenation. The magnitude of these effects varies widely between studies, and the current evidence in this regard is weak.<sup>4</sup> In recent years, HFOT has emerged as an alternative to NIV for respiratory support that is perceived as being easier to implement. Its use at the ward level has been proposed in patients with moderate to severe AB that meet the criteria for initiation of NIV, and there have been positive reports of its effectiveness in preventing the use of more aggressive modalities.<sup>5</sup> In the same way that this application of HFOT is considered useful, we believe that patients could benefit from NIV, which is both safe and efficacious, without in and of itself requiring admission to the PICU. The possibility of administering NIV at an early stage offers an added clinical benefit, as it may prevent progression of disease, thus reducing the mean length of stay of these patients.<sup>6</sup> We ought to note that the degree to which this technique was available in our hospital allowed a greater flexibility in its use, which may have contributed to NIV being prescribed in a greater proportion of the total admitted patients (19%) compared to other case series,<sup>3</sup> which in turn would have contributed to reducing the number of transfers.

The delivery of NIV in the inpatient ward is a feasible option that could help alleviate the problems that emerge every year during the AB season. The elements that we consider essential for its implementation are adequate training of the staff, the establishment of specific care protocols and the capacity to provide a safe environment and adequate care in case of clinical worsening until patients can be transferred to a PICU.

**Table 1** Epidemiological data and NIV settings used in the sample.

Epidemiologic data	N = 47
Male sex (%)	21 (44.7)
Birth <37 weeks (%)	11 (23.4)
Median age in days (p25–p75)	33 (18–51)
<b>Aetiological agent (%)</b>	
RSV	28 (59.6)
Other	19 (40.4)
HFOT (%)	17 (34)
Days elapsed from onset of NIV (mean, 95% CI)	4.5 (3.6–5.4)
<b>Indication for NIV (%)</b>	
Hypercapnia	17 (36.2)
Respiratory distress	8 (17)
Hypercapnia + distress	19 (40.4)
Apnoea	3 (6.4)
BiPAP (%)	6 (36.2)
<b>Duration of NIV (%)</b>	
<24 h	13 (27.7)
24–36 h	5 (10.6)
36–48 h	10 (21.3)
>48 h	19 (40.4)
Length of stay (mean, 95% CI)	5.9 (4.7–7.13)
Transfers to PICU (%)	16 (34)
<b>Reason for transfer (%)</b>	
Hypercapnia	9 (56)
Respiratory distress	4 (25)
Hypercapnia + distress	1 (6.2)
Apnoea	1 (6.2)
Other	1 (6.2)
<b>NIV settings (mean, 95% CI)</b>	
Max flow rate (L/min)	8.86 (8.5–9.31)
Max PEEP (cmH <sub>2</sub> O)	6.11 (5.57–6.3)
Max FiO <sub>2</sub> (%)	32.5 (27.9–38.1)
Max PCO <sub>2</sub> (mmHg)	59.2 (56.4–62.4)

BiPAP, bilevel positive airway pressure; FiO<sub>2</sub>, fraction of inspired oxygen; HFOT, high-flow oxygen therapy; IMV, invasive mechanical ventilation; NIV, non-invasive mechanical ventilation; PEEP: positive end-expiratory pressure; PICU, paediatric intensive care unit; RSV, respiratory syncytial virus.

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## Metabolic lactic acidosis as a sign of voluntary poisoning in adolescents<sup>☆,☆☆</sup>



### Acidosis metabólica láctica como manifestación de intoxicación voluntaria en adolescentes

Dear Editor:

Self-poisoning with suicidal intent accounts for 4.9% to 23.2% of poisoning cases managed in paediatric emergency departments in Europe.<sup>1</sup> It frequently involves multiple drugs, and in many instances it is not known which. The mainstay of management in these patients is stabilization, monitoring and supportive care, and it is essential to seek signs that may help identify the culprit substances to try to prevent potential toxicity.

Metabolic lactic acidosis usually develops in severely ill patients, and it is a marker of tissue hypoxia and an independent predictor of mortality.<sup>2</sup> In patients with poisoning, hyperlactatemia is also associated with poorer outcomes, although in most cases it is due to a direct toxic mechanism and may develop in patients that are clinically stable as an early marker of toxicity.<sup>2,3</sup> The management of lactic acidosis in the context of poisoning differs from its management in severely ill patients without poisoning. In the latter, management is based on respiratory and haemodynamic stabilization, while in poisoned patients it may be necessary to use some form of renal replacement therapy.<sup>3</sup>

We present the cases of 3 paediatric patients with metabolic lactic acidosis secondary to self-poisoning with suicidal intent (Tables 1 and 2). All patients were managed with monitoring of blood gases and administration of bicarbonate and fluids, to which they responded favourably. Two patients required admission to the paediatric intensive care unit (PICU) due to renal insufficiency or depressed level of

consciousness. The toxicology analyses identified the cause of the acidosis. The management included filing of a legal report and consultation with the psychiatry team.

Metabolic lactic acidosis can develop in the context of poisoning by metformin, nonsteroidal anti-inflammatory drugs (NSAIDs), salicylates, valproate, isoniazid, propofol or propylene glycol, among other substances, in both paediatric and adult patients.<sup>3</sup>

Metformin-associated lactic acidosis is rare and potentially severe. The underlying mechanism seems to involve the inhibition of pyruvate-dehydrogenase activity and suppression mitochondrial transport, which increases anaerobic metabolism and the production of lactate. It presents with nonspecific gastrointestinal symptoms, tachypnoea, tachycardia, arrhythmia, renal insufficiency or coma.<sup>4,5</sup> It has been described in diabetic patients with significant comorbidities and in adult patients with acute overdose, but few cases have been described in the previously healthy paediatric population, and all such cases have occurred in the context of suicide attempts. Hypoglycaemia does not usually develop unless other drugs are combined with metformin.<sup>4</sup> In case 1, the patient presented with lactic acidosis with renal insufficiency and hypoglycaemia.

In cases of NSAID poisoning, especially those involving ibuprofen and naproxen, metabolic acidosis results from the accumulation of the drugs themselves and of the acid metabolites derived from propionic acid, which cause an increase in the anion gap. Lactate elevation in these cases is moderate and probably secondary to hypoxia.<sup>6</sup> The most frequent manifestations are gastrointestinal, and neurologic manifestations (seizures or altered level of consciousness) are indicative of severe poisoning, as occurred in case 2. Patients may also develop renal impairment.<sup>6</sup> This picture has been described in paediatric patients with intentional poisoning with massive overdoses.

On the other hand, case 3 suggested that severe toxicity (lactic acidosis and renal insufficiency) may develop with the combined ingestion of metformin and a NSAID, even if the serum drug levels are not very high.

The initial management of metabolic lactic acidosis in these patients includes supportive care measures, clinical and electrocardiographic monitoring and serial arterial blood gas tests.<sup>2</sup> In most cases, treatment is based on fluid therapy and administration of bicarbonate. Some patients may require haemodialysis.<sup>2</sup>

There are few published data on serum drug levels in cases similar to those presented here. Metformin concentrations of 63.3 and 165 µg/mL and naproxen concentrations of 1290 µg/mL have been reported in the past, which are

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☆☆ Previous presentations: the results of this study were presented in part at the XXI Jornadas Nacionales de Toxicología Clínica and the XI Jornadas Nacionales de Toxicovigilancia, November 2017, Santiago de Compostela, Spain.