Survey of neonatal respiratory care and surfactant administration in very preterm infants in the Italian Neonatal Network

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Abstract. *Introduction:* Variation of respiratory care is described between centers around the world. The Italian Neonatal Network (INN), as a national group of the Vermont-Oxford Network (VON) allows to perform a wide analysis of respiratory care in very low birth weight infants. *Methods:* We analyzed the dataset of infants enrolled in the INN in 2009 and 2010 and, for surfactant administration only, from 2006 to 2010 from 83 participating centers. All definitions are those of the (VON). A questionnaire analysis was also performed with a questionnaire on centers practices. *Results:* We report data for 8297 infants. Data on ventilator practices and outcomes are outlined. Variation for both practices and outcome is found. Trend in surfactant administration is also analyzed. **Conclusions**. The great variation across hospitals in all the surveyed techniques points to the possibility of implementing potentially better practices with the aim of reducing unwanted variation. These data also show the power of large neonatal networks in identifying areas for potential improvement. (www.actabiomedica.it)

Key words: preterm infants, ventilation, ventilatory support

Introduction

Since 2005, the Italian Neonatal Network (INN) is collecting data following the Vermont-Oxford Network (VON) as national group. This program allows for a very wide monitoring of most important outcomes and procedures for very low birth weight infants. Among neonatal procedures, ventilation and respiratory care are of paramount importance. Survival increased in the last 30 years and advances in respiratory care are among contributors of these better outcomes. Nevertheless, variation of care is described between centers around the world (1-5); moreover, compliance with more recent standards of care deserve attention and monitoring. For these reasons, it is worth describing recent data on respiratory care in a wide national setting like the INN, with particular focus on ventilator support and surfactant treatment. A dual approach was adopted: (1) an analysis of the data of the respiratory support and care offered to individual very preterm neonates enrolled in the INN, and (2) a brief survey of the protocols in use in the neonatal units adhering to the INN.

Methods

We analyzed the dataset of infants enrolled in the INN in 2009 and 2010 and, for surfactant administration only, from 2006 to 2010. The INN is the Italian branch of the VON. It includes preterm neonates up to 29 weeks + 6 days of gestational age, or neonates with a birth weight <1501 g, admitted to any of the centers within 1 month of age. In 2009, 73 centers participated, and in 2010 a further 10 contributed data (Total = 83). The neonatal units participating in the INN care vast majority of very preterm infants in Italy, and in some Italian regions the coverage is complete. Therefore, the INN represents an important source of data that reflect neonatal management in Italy. All definitions are those of the VON (www.vtoxford.org); briefly, in addition to anthropometric measures such as gestational age (GA), birth weight (BW), sex, etc, the following variables are collected for each infant: respiratory management in the delivery room (use of oxygen, bag-and-mask ventilation, intubation, surfactant administration) and in the ward. As far as ventilator support is concerned, the database collects data on procedures such as oxygen supplementation; use of N-CPAP, of N-CPAP before intubation; of high flow nasal cannulae (HFNC); of nasal intermittent mandatory ventilation (N-IMV)/synchronized intermittent mandatory ventilation (SIMV); of conventional mechanical (CMV) ventilation; of HFV; and surfactant administration in the ward. Bronchopulmonary dysplasia (BPD) refers to the oxygen requirement at 36 weeks post conceptional age. The data of the INN is compared with the data from the whole VON in 2010 (more than 57 000 infants with the same characteristics), obtained from the web-based system "Nightingale". Questionnaire analysis was performed with a questionnaire prepared by PT and sent by email to all chiefs of neonatal units adhering to the INN, with reminders in case of non-response. It included questions on the existence in the unit of protocols detailing the approach to respiratory diseases in the neonates, and which type of respiratory support was chosen as first line therapy and whether HFV was used for rescue in the event of a failure of conventional mechanical ventilation. Fifty-seven hospitals (69%) responded.

Results

We report data for 8297 infants (3981 in 2009, and 4316 in 2010), treated in 83 hospitals (73 infants dying in the delivery room were excluded). The mean GA was 29.3 weeks (SD = 2.96) and the mean BW was 1089 g (SD = 302). Mortality was 14.2%, and BPD 13.9% (15.5% in infants <33 weeks).

Table 1 shows the percentage of infants receiving any of the listed procedures, comparing the data with the data from the VON.

The frequency of use of most procedures is lower in Italian hospitals in comparison to the VON. As INN recruits infants above 30 weeks GA only if they are below 1501 g BW, these procedures are displayed in Table 2 for infants of 23–29 weeks only (the data for this population is complete in the database). The GA-associated decrease in the use of procedures is clearly apparent.

Table 1. Percentage of infants receiving any of the listed procedures.

	INN	VON
Delivery room procedures		
Supplemental oxygen	76.2	85.3
Bag-and-mask ventilation	61.3	61.8
Tracheal intubation	41.4	50.8
Surfactant administration	16.8	32.3
After delivery room		
Oxygen	80.8	88.2
CMV	53.1	62.7
HFV	15.8	22.1
N-CPAP	71.5	68.2
N-CPAP before ETT	41.9	40.0
Any surfactant	56.1	63.1
HFNC	8.2	49.9
NIMV/NSIMV	17.6	18.7
Any mechanical ventilation	55.5	65.1
Non-invasive ventilation	71.7	–
Any respiratory assistance[a]	84.5	–
NIV only[b]	34.0	–

INN, Italian Neonatal Network; VON, Vermont-Oxford Network, 2010; ETT, endotracheal intubation; HFNC, high flow nasal cannula; NIMV, nasal intermittent mechanical ventilation; NIV, non-invasive ventilation; HFV, high frequency ventilation

[a]Ventilation or NIV, excluding oxygen supplementation.

[b]In infants receiving any respiratory assistance, excluding oxygen supplementation

Table 2. Percentage of use of selected methods of respiratory support according to GA, 23–29 weeks (%)

	Gestational age (weeks)							
	23	24	25	26	27	28	29	Total
DR surfactant	51.8	41.8	42.6	34.8	27.6	18.2	11.3	26.9
Any Surfactant	96.6	98.1	94.3	89.0	82.0	74.2	61.9	80.0
MV	99.6	99.4	96.0	90.6	80.8	67.4	53.0	76.6
NIV	36.4	56.9	70.8	83.6	87.7	89.0	87.2	80.0
Any Resp. assistance	99.6	100.0	99.5	99.6	99.5	97.4	93.7	97.7
NIV only	0.0	0.5	3.5	9.0	18.7	30.7	42.9	21.5

Table 3 provides details regarding surfactant administration; i.e. a comparison in the time to surfactant administration in infants of 23–29 weeks between INN and rest of the VON. For all GA weeks considered, the percentage of infants treated with surfactant >2 h of age is always greater in Italy than in the VON, even for very preterm infants, where surfactant is almost universally administered.

Among the different procedures and practices, a wide variation was observed among centers; the coefficient of variation was lower for non-invasive ventilation (0.17), ventilation (0.26) and delivery room intubation (0.36) than for CPAP before endotracheal intubation (ETT) (0.58), and was highest for HFV (0.86) and delivery room surfactant (0.89). It is difficult to ascribe this broad variation to differences in case-mix, and it likely represents a "physician-driven" variation.

Looking at annual trends for surfactant administration (data from 2006 to 2010), it is clear than in INN surfactant administration in lower than in VON. In the VON there is a slightly decrease of surfactant administration over time. In the INN surfactant administration is stable in the whole time period.

Table 4 shows comparative data on ventilator procedures (2006-2010). Considering other respiratory interventions in an homogeneous period (2006-2010, with no change in baseline risk), after adjusting for confounders, infants receiving invasive mechanical ventilation decreased ([OR]=0.74, 95% [CI] 0.58-0.97) while NIV increased (OR= 1.75, 95% CI 1.38-2.21); intubation in delivery room decreased (OR=0.61, 95%CI 0.5-0.75). Considering outcomes, there was a significant reduction in mortality (OR=0.71, 95% CI 0.54-0.94) and in the combined outcome mortality or BPD (OR=0.89, 95%CI 0.69-1.1).

Table 3. Surfactant administration (%) in INN and VON

	2006	2007	2008	2009	2010
INN	55,2	55,2	56,7	55,9	56,0
VON	64,2	64,0	63,8	63,6	62,9

Table 4. Frequency of selected ventilatory procedures

	2006	2010	p
Delivery room intubation	56.1%	48.1%	<0.001
nCPAP before intubation	28.8 %	45.2%	<0.001
Any ventilation	94.3%	96.7%	0.003
Mechanical ventilation	73.3%	66.4%	< 0.001
HFV	17.6%	22.9%	0.001
CMV	70.8%	64.7%	0.001
NIMV or SIMV	13.9%	25.18%	<0.001
NIV	76.9%	84.1%	<0.001
nCPAP	77.1%	84.5%	<0.001
HFNC	5.8%	16.6%	<0.001

HFV, high frequency ventilation; NIMV, nasal intermittent mechanical ventilation; NIV, non-invasive ventilation; HFNC, high flow nasal cannula

As for the results of the questionnaire, of the 57 hospitals that responded to the questionnaire, six said they did not have a protocol for respiratory assistance and were excluded from further analysis; all the others said that they used "non-invasive" techniques first.

In the event of needing tracheal intubation and mechanical ventilation as a first-intention treatment, two hospitals said they used IPPV/IMV; 20 synchronized IPPV/IMV (SIPPV/SIMV); 25 "volume guarantee" ventilation; and 10 hospitals used HFV (in five hospital for all infants, and in other five hospitals, depending upon BW/GA).

As for rescue HFV, seven hospitals (among those that did not always use HFV as a first intention) re-

sponded that they did not use HFV as a rescue, while all the others did use HFV as rescue.

Conclusions

This study represents a large scale, current survey of actual techniques used to provide respiratory assistance to very preterm infants, admitted to neonatal intensive care units in Italy in recent years. Our conclusions rest on more than 8000 very preterm/ very small neonates assisted in 83 centers in 2009–2010.

One major conclusion, in light of the current trend towards a lower level of invasiveness, is the number of infants who are managed without "invasive" (i.e. without endotracheal tube positioning) techniques. While invasive ventilation is always used at the lower extreme of viability, our data show that at 29 weeks, only half of the infants require intubation and receive at least one dose of surfactant, while the other half is managed non-invasively. The comparison with the data of VON shows that, on the whole, Italian neonates are treated less invasively.

In addition to the current description of use of various techniques, this study shows great variations in their use. This variation has been frequently reported (1-5]) in studies on ventilation. Despite the long time that HFV, CMV, and nasal continuous positive airway pressure (NCPAP) have been available, the differences between the centers are striking, and probably reflect different approaches to the preterm infants with respiratory distress, i.e. center -driven variation, rather than differences in case-mix.

The survey conducted among chiefs of neonatal units demonstrates that none of the respondents considers NIV unsuitable for a trial in infants. In practice, however, CPAP before intubation is used from 0% to about 80% of infants. As for the choice of invasive (with intubation) ventilation, only two hospitals used a non-synchronized "conventional" ventilation, five used HFV always, and the other five used HFV in some (smaller/more immature) infants only. The vast majority of units used synchronized ventilation, with or without volume guarantee.

It is worth noting that despite a stable baseline risk, from 2006 to 2010, we observed a lower level of invasiveness, a reduction of mechanical ventilation and an increase of NIV use, and this was accompanied by a decrease in risk-adjusted mortality and BPD.

These data form a basis for recognizing areas for potential improvement in ventilation given to preterm neonates.

The great variation across hospitals in all the surveyed techniques points to the possibility of implementing potentially better practices with the aim of reducing unwanted, center-related variation.

Last, these data show the power of large neonatal networks in identifying areas for potential improvement.

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[6] Appendix: Participants to the Italian Neonatal Network

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