Acta Biomed 2015; Vol. 86, Supplement 1: 11-15

Original article

Respiratory management of ELGA infants in a region of Southern Italy

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Summary. The distribution of births in many regions of Southern Italy is scattered among a high number of level I centers, many of which still count less than 500 deliveries per year. Campania, the region around Naples, is no exception and this excessive fragmentation results in a high number of neonatal transports, many of which for respiratory distress. In the present paper, we review three different regional peculiarities relevant to the respiratory management of extremely low gestational age babies. (www.actabiomedica.it)

Key words: respiratory management, preterm, ELGA infants

Introduction

With its 54 thousands yearly births, Campania, a southern region of Italy, accounts for 10.2 % of all Italian neonates. When compared to the North and the whole country, Campania has (1):

- a gradually decreasing neonatal mortality rate (2,5‰ in 2013) that approximates the national average (2,1‰) but still significantly higher than Lumbardy (1,7‰)
- a high number of level I birth centers that can assist only uncomplicated deliveries. In 2012 , level I centers were 56 accounting for 37.333 neonates while at the 14 Level II/III centers18.954 neonates were born.
- high number of caesarean section births (regional average 60% of all deliveries)
- high number of neonatal transports (about 1.500 neonates transported each year).

Indeed, there is sufficient evidence in the literature to believe that the above variables are connected in a network of questionable efficacy and efficiency.

The aim of this paper is to review those critical features of respiratory management of preterm and particularly of extremely low gestational age babies (ELGA 23-28 weeks) that might result from the present organizational pattern .

Respiratory assistance during transport of ELGA neonates

Three dedicated neonatal transport systems are simultaneously active serving an area of 13 670,95 km² and a population close to 6 million inhabitants. The already cited scattering of births contributes to a 2.6% global transportation index (a 1% index is considered the desired standard). Our transport team (Università Federico II) operated slightly more than half the 1446 transports from January 2012 and December 2013.

During this interval, 7.2 % of transported infants had a GA less than 30 weeks, a percentage that had been substantially stable across the years. When considering transported infants in need of respiratory support, out of a total 662 infants, 9% of were had a GA less than 30 weeks. This percentage was lower than the 11.8% recorded for the same class in the period 2004-2007.

As per the respiratory assistance mode during transport in the 2012-2013 period, 20 ELGA neonates received IPPV, 5 had nasal CPAP and 9 had plain oxygen therapy in the incubator.

While we detect a trend in decreasing the transports of ELGA neonates along the years, we affirm that the optimal result would be no transport at all. Low gestational age confers an additional risk of moving a baby from her/his birthplace. The low intensity of respiratory support offered to 14/34 neonates speaks in favour of relatively stable conditions and possibly short trips. One more reason to suggest birth centralization to our health policy makers.

Data from the Campania section of the Vermont Oxford Database

The latest, 2013, ELGA cohort available from the Campania section of the Vermont Oxford Network (VON) consists of 208 preterm infants between 22-29 weeks gestational age (Table 1). Their mean mortality 30.3% (IC: 22.2 – 33.3%) was higher than the Italian section of VON (Italian Neonatal Network, INN) that shows a mean mortality of 22.7% (IC: 14.3-30.6). Considering infant characteristics at admission, 87.4% of babies are inborn (INN: 90.5%), 82.5 % received prenatal care (INN: 90.3%), chorioamnionitis rate is 13% (INN: 19.1%), maternal hypertension 21.4% (INN: 18.2%), antenatal steroids were used for 60.4% of babies (INN: 80.3%), 15.3% of babies were SGA (INN: 12.4%).

Looking at the initial resuscitation in delivery room of such small babies, in Campania the mean incidence of Apgar score < 4 at five minutes of live was 5.7% similar to the INN incidence (6.1%). Delivery room deaths were 2.3% in Campania and 1.5% in Italy. The delivery room resuscitation management in Campania included: face mask ventilation 50% (INN: 72.1%), cardiac compression 14% (INN: 9.8%), surfactant 11.3% (INN: 21.8 %), epinephrine 10.3 % (INN: 4.9%), intubation 73.4% (INN: 57%), oxygen 80.4% (INN: 85.6%), CPAP in delivery room: 13.6% (INN: 39.4%).

Respiratory distress syndrome was diagnosed in 96.2% of these babies in the Campania cohort (90.2% INN).

Mechanical ventilation was used for 88.6% of babies during hospital staying (conventional 86.2%, high frequency 46.7%) in Campania while INN data show that mechanical ventilation was used for 73.2% of babies during hospital staying (conventional 68.7%, high frequency 28.5%).

In Campania, CPAP was used for 69.5% of babies during hospital staying (but CPAP before intu-

Table 1. Respiratory care during neonatal transport in Campania for 2012 - 2013 compared with years 1995 - 2007. Data from University "Federico II" neonatal transport database

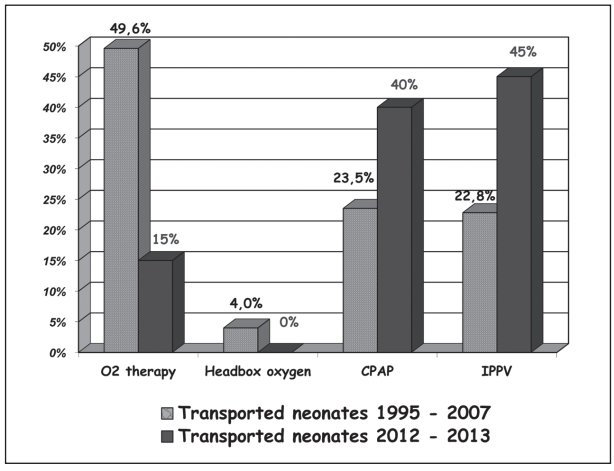
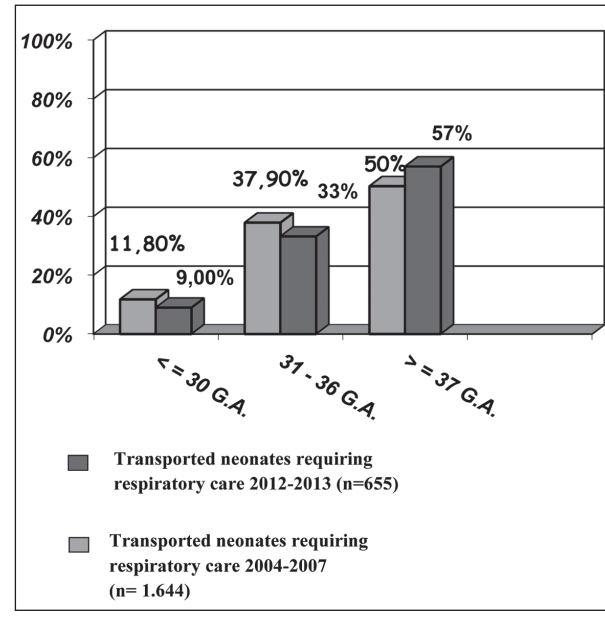


Table 2. Transported neonates requiring respiratory care divided by GA for 2012 - 2013 compared with years 2004 - 2007. Data from University "Federico II" neonatal transport database



bation only 24.8%) while in the INN cohort CPAP was applied to 77.4% babies during hospital staying (and 48.7% before intubation). High flow nasal cannula was used for 8.6% (INN: 30.3%) babies and nasal IMV/SIMV 25.7% neonates (INN: 31.6%)

Surfactant at any time during hospital staying was administered to 85.8% of babies in Campania and 74.7% in the INN. In Campania 63.8% of babies have received surfactant in the first 2 hours of life (INN: 44%).

While the incidence of pneumothorax (2.9% IC: 0-5.9%) was significantly lower than the INN data (5.2% IC: 0-8.1%), both the incidence of chronic lung disease (Campania 29.5% vs INN 26.1%) and the use of steroids for chronic lung disease (Campania 17.9% vs INN 17.3%)) were comparable. Inhaled nitric oxide was used for 1% of babies in Campania and for 5% in the INN. In the year 2013, 6.1% of babies were discharged home on oxygen in Campania (8.9% for INN).

Taken together, the data suggest that ELGA infants are being born in suboptimal conditions in our region. In fact, figures from the Campania VON section (including data from 10 of 15 NICUs), show less prenatal care, much less antenatal steroids, have higher frequency of maternal hypertension and SGA compared to INN. All these conditions may contribute to explain the higher mortality rate, the more aggressive respiratory approach in the delivery room management and in the respiratory management during hospital stay of ELGA infants in Campania. Conversely, the lower figures for pneumothorax in Campania might be related to a less extensive use of N-CPAP with reduced mean airway pressure.

Strategies to improve outcomes of ELGA infants need to improve both prenatal care, and the use of pre-

Table 3. Characteristics of preterm infants with GA 22 - 29 weeks included in the Campania section of VON compared to the Italian group of VON (INN)- year 2013

	VON Campania (N = 208)	NN (N = 2.187)
Mortality	30,3%	22,7%
Inborn	87.4	90.5
Prenatal care	82.5	90.3
Chorioamnionitis	13%	19.1%
Maternal hypertension	21.4%	18.2%
Antenatal steroids	60.4%	80.3%
Apgar score <4 at 5'of life	5,7%	6,1%
SGA	15.3%	12.4%
Delivery room deaths	2,3%	1,5%
Face mask in delivery room	50%	72,1%
Cardiac compression in delivery room	14%	9,8%
Surfactant in delivery room	11,3%	21,8%
Epinephrine in delivery room	10,3%	4,9%
Intubation in delivery room	73,4%	57%
Oxygen in delivery room	80,4%	85,6%
CPAP in delivery room	13,6%	39,4%
Respiratory distress syndrome	96,2%	90,2%
Mechanical ventilation	88,6%	73,2%
N-CPAP during hospital staying	69,5% (N-CPAP before intubation 24,8%)	77,4% (N-CPAP before intubation 48.7%)
High flow nasal cannula	8,6%	30,3%
Nasal IMV/SIMV	25,7%	31,6%
Surfactant at any time	85,8% (in the first 2 hours of life 63,8%)	74,7% (in the first 2 hours of life 44%)
Pneumothorax	2,9%	5,2%
Chronic lung disease	29,5%	26,1%
Steroids for chronic lung disease	17,9%	17,3%
Inhaled nitric oxide	1%	5%
Babies discharged home with oxygen	6,1%	8,9%

Table 4. Main characteristics and extubation failure rate within first week in preterm neonates assisted in n-cpap versus bi-level n-cpap (BiPAP) after extubation

	nCPAP	BiPAP	p
GA (wks)	29±1.9	27.5±2.7	<0.05
BW (gr)	1.071±246	854±229	<0.05
Extubation failure	43	23	0.766
Extubation failure within the first week	25	5	<0.05

natal steroids. The transportation of such immature infants should become an exceptional event by promoting "in utero" transport of all at risk of preterm birth to an adequate number of NICU beds.

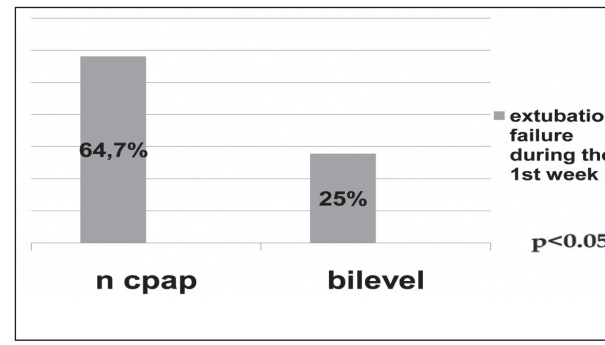
At the same time, neonatologists needs to put all efforts to implement the systematic application of early non-invasive ventilation starting from the delivery room with selective surfactant administration and rapid extubation to reduce rates of mechanical ventilation, postnatal steroid therapy and ultimately chronic lung disease as recently recommended by AAP (2).

Use of Bi-level vs nasal CPAP as a respiratory support mode after extubation of VLBW and ELGA infants

Finally, we present the preliminary data from a retrospective study conducted in the NICU of the University "Federico II" in Naples, from January 2009 to December 2013. Although all VLBW infants intubated at birth were enrolled in this study, for the purpose of this paper we also extrapolated the data of ELGA infants.

The study primary aim was to compare the rate of failure of nCPAP (PEEP 4-5 cm H2O) versus bi-level (PEEP 4-5, PIP 7-8 cm H2O, it 0.7-1, rate: 10-40/min) as non-invasive respiratory support after extubation of VLBW infants with respiratory distress syndrome. Failure of n-cpap and bi-level was defined as the need of more intensive respiratory support (bi-level or intubation and mechanical ventilation for the nCPAP group and intubation and mechanical ventilation for the bi-level group). The indications to switch to a higher intensity of respiratory support were: worsening of clinical signs of RDS, inability to maintain oxygen saturation between 85-95% and respiratory acidosis (pH < 7.25 and PaCO2 > 65 mmHg). Secondary outcomes were: rate of failure of nCPAP versus BiPAP within the first week from extubation, mortality, pneumothorax, PVL, BPD and ROP at discharge; 146 babies were enrolled (97 in n-cpap group; 49 in bi-level group). No difference was found in the demographic variables except for birth weight and gestational age (GA): 1.071 ± 246 gr, GA 29± 1.9 in nCPAP group vs 854 ± 229, GA 27.5 ± 2.7 in bi-level group (Tab. 1). Extubation failure during the first week was more frequent in n-cpap group: 25/97 (25.7%) vs 5/49 (10.2%) in bi-level group (p<0.05) (table 1). Extrapolating data for infants between 22 – 29 weeks of GA, 22/34 babies (64.7%) in n-cpap group vs 5/20 (25%) in bi-level group (p<0.05) failed extubation during the first week (graph 1). No difference was found for the other outcomes for infants between 22-29 weeks of GA.

The early use of nasal ventilation has been extensively promoted in the last decade starting from delivery room resuscitation (4) and different modes of support have been proposed. Beyond the classical nCPAP, the BiPAP, i.e. two different nasal pressure during spontaneous respiration, has gained popularity. Unlike CPAP, BiPAP may generate a tidal volume that improves gas exchange. On the other hand, the success of BiPAP over n-CPAP in our setting may be related to the higher mean airway pressure delivered without difference in rate of pneumothorax. This is in keeping with the recent observation by Buzzella studying very preterm infants (23-30 weeks) that higher distending



Graph 1. Extubation failure within first week for preterm infants between 22 - 29 weeks of GA assisted in nCPAP vs BiPAP after extubation

pressures are needed post– extubation for the more immature infants (3).

In 2010 Lista in a small RCT showed that preterm babies assigned from birth to bi-level compared with n-cpap for treatment of RDS had less need of respiratory support and fewer oxygen dependency days (5). In the same year, Ancora et al published a retrospective study showing that bi-level compared with nCPAP reduced the need for mechanical ventilation in the 7 days after Insure failure in VLBW infants (6). Recently, an Italian RCT in VLBW infants showed no statistically significant differences for bi-level compared with nSIPPV as primary treatment of RDS in the first 2 hours of life in terms of duration of ventilation and failure, suggesting that both NIV techniques are effective in the early treatment of RDS in VLBW infants (7).

Given the relatively high number of VLBW who are still mechanically ventilated, a direct comparison post extubation of nasal ventilation techniques was needed. Our data, although retrospective, contribute to fill this gap together with future larger, prospective studies.

References

1. Università di Napoli Federico II. Regione Campania. "Rapporto sulla Natalità in Campania anno 2012". http://www.epicentro.iss.it/problemi/percorso-nascita/pdf/pdf%20rapporto%202012.pdf
2. AAP Committee on Fetus and Newborn. Respiratory Support in Preterm Infants at Birth. Pediatrics 2014; 133; 171.
3. Buzzella B, Claure N, D'Ugard C, Bancalari E. A Randomized Controlled Trial of Two Nasal Continuous Positive Airway Pressure Levels after Extubation in Preterm Infants. The Journal of Pediatrics 2014; 164: 46.
4. Capasso L, Capasso A, Raimondi F, Vendemmia M, Araimo G, Paludetto R. A randomized trial comparing oxygen delivery on intermittent positive pressure with nasal cannulae versus facial mask in neonatal primary resuscitation. Acta Paediatr 2005 Feb; 94 (2): 197-200.
5. Lista G, Castoldi F, Fontana P, Daniele I, Cavigioli F, Rossi S, Mancuso D, Reali R. Nasal continuous positive airway pressure (CPAP) versus bi-level nasal CPAP in preterm babies with respiratory distress syndrome: a randomised control trial. See comment in PubMed Commons below. Arch Dis Child Fetal Neonatal Ed 2010 Mar; 95 (2): F85-9.
6. Ancora G, Maranella E, Grandi S, Pierantoni L, Guglielmi M, Faldella G. Role of bilevel positive airway pressure in the management of preterm newborns who have received surfactant. Acta Paediatr 2010 Dec; 99 (12): 1807-11. doi: 10.1111/j.1651-2227.2010.01910.x.
7. Salvo V, Lista G, Lupo E, Ricotti A, Zimmermann LJ, Gavilanes AW, Barberi I, Colivicchi M, Temporini F, Gazzolo D. Non invasive ventilation strategies for early treatment of RDS in preterm infants: an RCT. Pediatrics 2015 Mar; 135 (3): 444-51.

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