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Original article

Acute respiratory failure in children: epidemiological data from the Italian Network of Pediatric Intensive Care Units

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Abstract. *Introduction:* observational prospective multicenter study to describe the incidence of ARF in Italian PICUs. *Materials and Methods:* all children aging 0-16 years admitted in 13 Italian PICUs over one year. *Outcomes:* 2267 children were analyzed. ARF is the most common reason for admission in PICUs and about one children over two receive mechanical ventilation. ALI/ARDS incidence is 6,5% with a mortality rate of 30%. *Discussion/Conclusions:* the incidence and mortality of ALI/ARDS in PICUs in Italy are similar to those published by other studies. Surfactant is still a promise therapy for children and should be investigated for its potential benefit. (www.actabiomedica.it)

Key words: children, mechanical ventilation, ARF, ARDS

Introduction

Acute respiratory failure (ARF) in children is one of the most frequent diagnosis of hospital admission (1). The most common reason for ARF in children is an infection mainly in the lower respiratory tract. Indeed bronchiolitis and pneumonia are the most common diagnosis for ARF in PICUs (2). Among patients with ARF, Acute Lung Injury (ALI) and Acute Respiratory Distress Syndrome (ARDS) represent the most severe forms with the highest morbidities and mortalities. In adults, the ARDS rate is estimated as 78.9/100000 patients per year with a mortality of 40% (3).

For the paediatric age, although the definitions of ALI/ARDS are the same as for adults (4), few studies have been published describing prospectively the epidemiology and treatment in large populations (5, 6). Most of the authors reported a single center experience or retrospective data and there are few interventional clinical trials (7, 8). One reason for the lack of evidence in children is that although there are some similarities in pathophysiology and risk factors between adult and children (9), ALI and ARDS are less common in children than in adult. Moreover, when a large trial was designed, the feasibility to enroll enough patients was low (10).

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From the few data available, the ALI/ARDS rate is estimated between 2.2 and 12/100000 children per year and the incidence increases with age. About 1-4% of the children admitted to PICUs and 8-10% of those mechanically ventilated have ALI/ARDS and the mortality is lower than in adults and runs between 20 and 75 % according to different studies. In Italy no epidemiological data are available on ARF. Since 2010, a network of 13 Italian PICUs prospectively records data of all patients admitted in their units for epidemiological, quality and research reasons with a specific case report form (CRF) on mechanical ventilation. Aim of this prospective observational multicenter study is to describe rate, reason, morbidity and mortality of children with ARF admitted to these PICUs during 2011.

Materials and methods

We used data from the national permanent database of the Italian PICUs Network (TIPNet) which collects data from all the patients admitted in 13 medical/surgical units all over the country. Data were collected from January 2011 to December 2011 through a web based data management system. We analyzed all the children aging 0-16 years admitted to PICU. Exclusion criteria were newborn and children older than 16 years. The database collects the following data: demographic data (gender, age, race, weight), descriptive data (typology, origin, reason for admission, comorbidity) outcome data (length of PICU stay, severity score on admission, mortality rate both raw and standardized). As severity score on admission we use the PIM2 score. For all the children who underwent mechanical ventilation either invasive (ETI) or noninvasive (NIV), a specific CRF was used with details on kind of ventilation (ETI, NIV or both), timing (before PICU stay, within 1 hour from PICU admission or during PICU stay), length of ventilation. Ventilation change as passage from noninvasive to endotracheal intubation or the other way around were recorded. As reason for mechanical ventilation, a multi choice field was available. ALI and ARDS were defined according to the international Consensus Conference definitions (3). The use of surfactant was also recorded. Data are shown as mean with standard deviations (SD), medians with interquartile range (IQR), and proportions, as appropriate.

Outcomes

3242 patients were recorded in the database. Of these, 3170 (96.2 %) were available for analysis because fully included. This population represents the 76,9 % of the total number of children (n = 4123) enrolled by the 13 PICUs. 4 units participated for only 6 months instead of the entire year due to administrative reason. 712 patients were excluded because newborns while 191 were excluded because older than 16 years. 2267 children were therefore analyzed. The F/M ratio was 0,68 with a mean age of 48,23 months (median 23,84). Most of the patient were Caucasian (85,5%). Description of the cohort is presented in table 1. 967 children (42,6%) have a comorbidity mainly a neurologic disease (63,4%). 1108 children (48,9%) received mechanical ventilation (MV): 891 (80,4%) had only invasive ventilation (ETI), 209 (18,9%) were treated only with noninvasive ventilation (NIV), 103 (9,3%) received invasive ventilation first and noninvasive ventilation as weaning purpose or to avoid reintubation (ETI+NIV) and 32 (13,2%) received noninvasive ventilation first and were intubated because of NIV failure (NIV + ETI). 764 children (61,9%) started mechanical ventilation before PICU admission while 278 (25,1%) within the first hour of PICU admission. 193 (15,6%) started ventilation during PICU stay. Table 3 show the starting time of MV for each pattern of ventilation.

Respiratory failure was the most frequent reason for admission among medical patients (603 children, 52.2%) while among children admitted for trauma, 24 (16,4%) had respiratory failure. As primary reason for mechanical ventilation, postoperative care was the most frequent choice (371 children, 33,5%). 274 children (24,7%) had lower respiratory tract infections: pneumonia (n = 185) and bronchiolitis (n = 89). ARDS and ALI were recorded in 55 (4,9%) and in 25 children (2,2%) respectively. Other diagnosis which required MV were altered consciousness (n = 162) and muscular weakness (n = 135). Surfactant was used in

Table 1. Description of the overall population enrolled in the database during 2011

	Overall	Non ventilated	Ventilated
N	2267	1159	1108
Gender (F/M)	0,67	0,66	0,67
Age category:			
Neonate	4,6	4,6	4,3
Infant	30,7	32,0	29,4
Preschool	32,9	32,3	33,4
School	21,8	20,7	22,8
Adolescent	10,1	10,2	9,9
Origin:			
Other origin	3,2	3,6	2,6
Other hospital	22,5	16,1	31,6
Home	3,8	4,3	3,1
Hemodynamic	1,0	1,1	0,7
ER	14,6	14,8	14,4
Ward	17,2	19,2	14,5
OT	37,6	40,8	33,0
Typology:			
Surgical	42,6	46,7	36,8
Medical	51	47,7	55,6
Trauma	6,4	5,5	7,6
Immunocompromized	4,8	4,1	5,0
Comorbidity	42,6	42,9	42,4
Mortality	4,6	1,8	7,5
SMR	0,89	0,74	0,93

ER = emergency room; OT = operating theater; SMR = standardized mortality rate

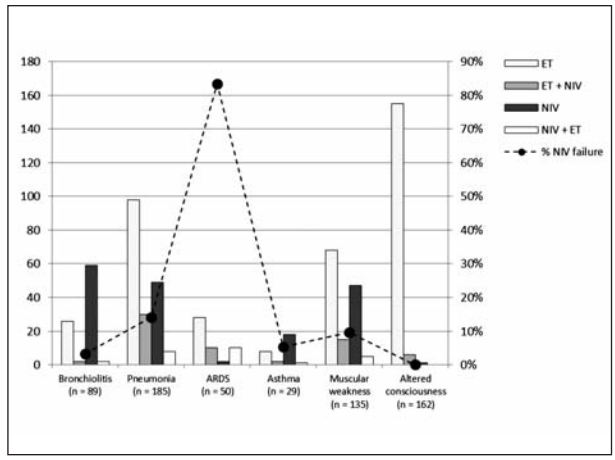

Figure 1. Modes of ventilation for different ARF diagnosis

23 children (2,1% of all children receiving mechanical ventilation) mainly in infants (n = 13) and preschool children (n = 10). 17 patients treated with surfactant (73%) had ARDS. Inhaled nitric oxide (iNO) was used in 26 (2,2%). Mean duration of ventilation was 6,8 days for ET and 4,4 days for NIV. Figure 1 shows the different modes of ventilation for specific diagnosis of ARF. Mortality rate of the overall population was 4,4% with an SMR of 0,86 while mortality rate for children with respiratory failure was 7,7 (SMR

Table 2. Starting time of MV for different ventilation pattern

	ETI	ETI + NIV	NIV	NIV + ETI
Before PICU admission	650	77	31	6
On admission (within 1° hour) in PICU	130	12	127	9
During PICU stay	111	14	51	17

ETI = endotracheal intubation; NIV = noninvasive ventilation

Table 3. Frequency and median ventilation days for different ARF causes and ventilation mode

	ETI		ETI + NIV		NIV		NIV + ETI	
	n	Ventilation days	n	Ventilation days	n	Ventilation days	n	Ventilation days
Bronchiolitis	26	5	2	-	59	2	2	-
Pneumonia	98	6	30	4 + 2	49	3	8	1 + 5
Asthma	8	3,5	2	-	18	1	1	-
ARDS	28	6	10	8,5 + 3	2	-	10	1 + 8
Muscular weakness	68	8	15	3 + 3	47	3	5	3 + 7
Altered consciousness	155	1	6		1	-	0	-
Post operative	**426**	**1**	**41**	**1 + 1**	**10**		**2**	-

ETI = endotracheal intubation; NIV = noninvasive ventilation

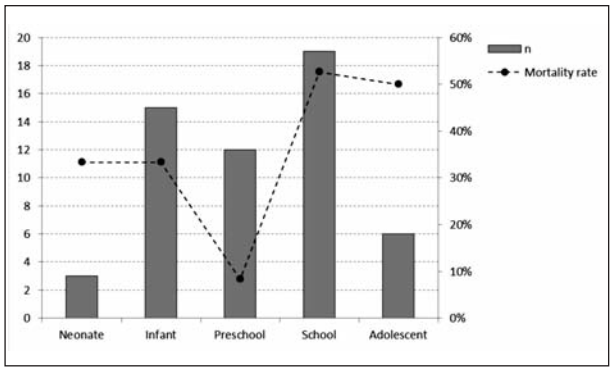

Figure 2. ARDS distribution and mortality rate for age categories

0,93). ARDS mortality rate was 36,4% (20 children) with an SMR of 2,7. 35 (63,6%) children with ARDS had chronic underlying disease with a mortality of 48,6%. 15 (27,3%) were immuno compromised with a mortality of 53,3%. Mortality among children with ARDS who received surfactant (n = 17) seems to be lower than among patients not receiving surfactant (n = 38), but data are not sufficient to correctly compare the two groups.

Discussion

Our data show that almost one every two children admitted in Italian PICUs need mechanical ventilatory support. If we exclude postoperative children, low respiratory tract infections represent the most common reason for mechanical ventilation. Although NIV diffusion is now increasing in PICU, most of the children still undergo tracheal intubation and receive invasive ventilation. This is the result of two elements: different habits among PICUs and the time of MV beginning. Some units did not use NIV at all, either as first treatment option either for weaning purpose or to avoid re-intubation. In units where NIV is commonly used, it represent the first option whenever possible. We have compared these data with those collected five years ago in the same units (unpublished data), and we have found an increase of NIV use (from 12 to 22%, $p<0,05$) with a slight increase of NIV failure (from 10 to 14,5%, p = ns). Nevertheless, there was not a more homogeneous diffusion of NIV use among the country, which means that those who already have expertise in NIV are more and more confident with its use.

Table 4. Comparison with published studies

	Costil (1995)	Goh (1998)	Flori (2004)	Dahlem (2007)	ANZICS (2007)	Italy
# center and length of the study	Multicentric 2 yrs	Single center 2 yrs	2 centers 2-4 yrs	single center	Multicentric 1 yr	Multicentric 1 yr
N of patient	N = 123	N = 21	N = 320	N = 44	N = 117	N = 50
Entry criteria	MV, FiO2 0.5, chest x-ray	LIS-AECC (ARDS)	AECC	AECC e MV	AECC e MV	AECC
Incidence (% of admission)	2%	4.2%	NA	4%	2.2%	2,3%
Etiology	Pneumonia 65% Sepsis 16%	Sepsis 43% Pneumonia 33%	Pneumonia 35% Sepsis 13%	Sepsis 34% Bronchiolitis 16%	LRTI 56% Sepsis 19%	LRTI 70%
Mortality	60%	62% (ARDS)	22% (ARDS 29%)	27% (ARDS 31%)	35% (ARDS 39%)	ARDS 38%
Related factors to mortality	P/F ratio	P/F ratio MOF PRISM score	P/F ratio MOF pH	P/F ratio MOF PRISM score	P/F ratio-OI MOF pH	Immuno-compromisation

LRTI = lower respiratory tract infection; P/F = Pao2/FiO2 ratio; MOF = multiple organ failure; AECC = American European consensus conference; MV = mechanical ventilation; OI = oxygenation index

If we analyze when MV is started, we observe that most of the children are ventilated before PICU admission rather than during PICU stay. ETI is prevalent in children who started MV before the admission in PICU both for surgical and medical patient. Surgical children come from the operation room still intubated for weaning, while medical patient with ETI are mainly transferred from other hospitals and intubation is often a protective strategy during inter-hospital transport. Indeed, almost 50% of these children are extubated within 24 hours from PICU admission.

Surfactant: This study was not calibrated to obtain specific information on how surfactant is used in the Italian PICUs. We have only registered that the drug is used mainly in infants and small children and that the main indication was ARDS. Data on the outcome of these children are not comparable. Potential benefits need to be investigated.

PICU overall mortality is low in children (4,4%) but it is almost doubled when respiratory failure is the reason of admission (7,7%). Our data are similar to those already published in other studies (Tab. 4) both for frequency and mortality of ARDS among ventilated children. ARDS represents one of the highest causes of death in PICU and the outcome depends on the underlying health status of the patient (11). In particular, immunocompromized children with ARDS have the highest risk of death (67%). This is an observational survey that did not collect data on how the patients were ventilated, if a protective lung strategy or the prone position were used. Because of the high mortality rate of ARDS a future prospective interventional study should be useful in order to understand the efficacy of specific treatment and which factors are related with a positive outcome.

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