Clinical epidemiological investigation of acute lung injury and acute respiratory distress syndrome in children

Lu-Qi Zhu and Xia Chen

Nanchang, China

***Background*: Few epidemiological studies on pediatric acute lung injury (ALI) or acute respiratory distress syndrome (ARDS) have been published. This investigation aimed to understand clinical epidemiological situation of ALI and ARDS in China.**

***Methods*: A series of 64 patients with ALI hospitalized at the pediatric intensive care unit (PICU) of our hospital from February 1996 to January 2001 was analyzed by case-control study. Six death risk factors were studied by single-factor relative risk analysis.**

***Results*: All 64 patients accounted for 0.084% of total hospital admissions and 3.77% of critically ill patients at the PICU during the same period, with an increased morbidity and a mortality of 34.38%. In primary intra-pulmonary diseases, pneumonia was predominant, followed by inhalation. Extra-pulmonary diseases were mainly due to sepsis and heat-stroke syndrome. The order of 6 death risk factors included systemic inflammatory response syndrome (SIRS), extra-pulmonary organ dysfunction, $PaO_2/FiO_2 \leqslant 200$, sepsis, critically ill score $\leqslant 70$, and pneumonia.**

***Conclusions*: The morbidity of ALI/ARDS is increasing because of improved recognition and diagnosis of the disease. The mortality remains high, while SIRS developing into multiple organ dysfunction syndrome is a high-risk factor causing death.**

World J Pediatr 2005;2:117-120

***Key words*: pediatrics;
acute lung injury;
acute respiratory distress syndrome;
epidemiology**

Author Affiliations: PICU, Jiangxi Children's Hospital, Nanchang 330006, China (Zhu LQ and Chen X)

Corresponding Author: Lu-Qi Zhu, MD, PICU, Jiangxi Children's Hospital, Nanchang 330006, China (Tel: 86-791-6813603; Email: zhuluqi@swissinfo.org; jxzhuluqi@163.com)

Introduction

In the pediatric intensive care unit (PICU), the death of critically ill patients is not due to primary diseases but multiple organs dysfunction syndrome (MODS) developed from systemic inflammatory response syndrome (SIRS). As the first target organ, lung often presents with acute lung injury (ALI) and its advanced phase, acute respiratory distress syndrome (ARDS). Even with intensive vital organ supports and treatment of anti-inflammatory and primary diseases, the mortality of ARDS remains as high as 48%-75% in adult ARDS. Few epidemiological studies have been published on pediatric ALI/ARDS worldwide.[1-4]

Methods

Diagnostic criteria

ALI/ARDS was diagnosed according to the criteria of the American-European Consensus on ARDS of 1994.[5] SIRS was determined according to the criteria set up at the Second World PICU Conference in 1996.[6] The patents were scored and MODS was diagnosed according to the "pediatric critically ill scoring system and pediatric system organ failure diagnosis" developed at the national Taiyuan meeting in 1995.[7]

Patients

Among the 64 patients with ALI/ARDS, 42 were male and 22 female, with the youngest being 30 days old and the eldest 11 years old. Twenty-three patients had critically ill score $\leqslant 70$, and 59 met the SIRS criteria. Five non-SIRS patients varied in age from 30 to 40 days. In terms of primary diseases, 25 patients were due to intra-pulmonary factors and 39 extra-pulmonary factors. $PaO_2/FiO_2 \leqslant 200$ (ARDS) was found in 54 patients, and PaO_2/FiO_2 201-300 (ALI) in 10. In 53 patients (82.8%) with extra-pulmonary involvement,

24 had 2 organs involved (including lungs) and 29 more than 2 organs involved. Twenty-seven patients received nasal continuous positive airway pressure (NCPAP) respiratory support, 19 mechanical ventilation, 15 high frequency jet, and 3 mask supply. Twenty-two patients (34.4%) died.

Epidemiological analysis

Hospital and PICU admissions, the morbidity, mortality and main primary diseases of ALI/ARDS in the same period were analyzed to understand their changes.

Six death risk factors were related to the mortality of ALI/ARDS, including etiology, critically ill scoring, SIRS, extra-pulmonary involvement and PaO_2/FiO_2.

Statistically a case-control study was conducted to analyze single factor odds ratio (OR). Twenty-two patients died and 42 controls survived.

Results

The patients with ALI/ARDS accounted for 0.084% of a total of 76 114 patients hospitalized during the same period; the yearly morbidity was 0.04%, 0.044%, 0.067%, 0.12% and 0.13%, respectively from 1996 through 2000. ALI/ARDS accounted for 3.77% of 1698 children admitted to PICU whose critically ill score was ≤80 in the same period; the yearly PICU morbidity was 1.57%, 1.65%, 2.87%, 6.08% and 9.47%, respectively for each year.

The primary diseases and 6 death factors of the 64 patients with ALI/ARDS are listed in Tables 1 and 2. Pneumonia was the main intra-pulmonary disease which accounted for 0.12% of total hospital pneumonia admissions during the time, then followed by inhalation (smoke, poisoning gas, swimming pool water, gastric contents); sepsis was the main extra-pulmonary disease and accounted for 0.65% of total sepsis hospital admissions, followed by infant heat-stroke syndrome.

Of the 64 patients, 22 (34.38%) died, including 1 (10%) of 10 patients with ALI, 21 (38.89%) of 54 patients with ARDS. Six of 22 patients with NCPAP support (22.22%) died, 12 (63.16%) of 19 patients with mechanical ventilation, 3 of 15 patients with high frequency support, and 1 of 3 patients with mask oxygen supply. SIRS was the highest among 6 death risk factors in all 22 fatal patients (Table 3).

Table 1. Primary diseases of the 64 patients with ALI/ARDS

Group	*n*	Intra-pulmonary			Extra-pulmonary						
		Pneumonia	Inhalation	Contusion	Sepsis	Heat-stroke syndrome	Severe enteritis	Epileptic state	Poisoning	Intracranial hemorrhage	Post-operation of liver rupture
Fatal	22	5	0	2	10	2	2	0	0	1	1
Survival	42	11	7	0	6	8	2	4	3	0	0
χ^2 value		0.092	2.584	1.510	7.481	0.462	0.018	0.905	0.438	0.110	0.110
P		0.761	0.108	0.219	0.006	0.497	0.892	0.341	0.508	0.740	0.740

Table 2. Six death factors of the 64 patients with ALI/ARDS

Group	*n*	Pneumonia	Sesis	SIRS	MODS	PaO_2/FiO_2	Critically ill score ≤70
Fatal	22	5	10	22	21	20	12
Survival	42	11	6	37	32	33	11
χ^2 value		0.092	7.481	1.428	2.532	0.999	2.880
P		0.761	0.006	0.232	0.112	0.371	0.090

Table 3. Logistic regression analysis of death risk factors of ALI/ARDS

Risk factors	Regression coefficient	Standard error	χ^2	*P*	OR	95% confidence interval
SIRS	7.928	24.869	0.102	0.750	>100*	$0.000\text{-}4.09\times10^{25}$
MODS	1.669	1.173	2.024	0.155	5.308	0.533-52.910
Sepsis	1.533	0.681	5.065	0.024	4.634	1.219-17.614
Critically ill score ≤70	0.628	0.646	0.944	0.331	1.873	0.628-6.641
PaO_2/FiO_2 ≤200	0.370	0.965	0.147	0.701	1.448	0.218-9.604
Pneumonia	0.178	0.720	0.061	0.805	1.195	0.291-4.899

*: OR value ∞, expressed by >100.

Discussion

The reported morbidity of ARDS in PICU was around 1%[5], but it is unclear among the pediatric population.[8-11] In this study, the morbidity of ALI/ARDS and ARDS in PICU were 3.77% and 3.18% respectively, which were higher than those previously reported. In this hospital, it was 0.084%, and was increasing yearly in the five-year period because of the improved recognition and diagnosis. The exact morbidity may be higher since some patients were misdiagnosed as having severe pneumonia, heart failure, or acute lung edema and not transferred to PICU. Therefore, pediatricians must better understand the disease, and transfer patients to PICU in a timely manner.

Extra-pulmonary diseases were predominant in causing ALI/ARDS in this study, especially sepsis and heat-stroke syndrome. Intra-pulmonary diseases, pneumonia and inhalation,[12] are different from sepsis, severe pancreatitis, inhalation of gastric contents, chest and abdominal trauma, and multiple bone fracture reported in adults.[5,13] The morbidity of ALI/ARDS in sepsis and pneumonia was 0.65% and 0.12% respectively in this study. There were no comparable reports, only Dobyns[14] reported that 20%-40% of sepsis cases may develop ARDS; but the rate was much higher than that in this study because of a different definition of sepsis.[15]

The order of the 6 risk factors defined by relative risk (RR) of death, single factor analysis, was as follows: SIRS, extra-pulmonary organ dysfunction, $PaO_2/FiO_2 \leqslant 200$, sepsis, critically ill score $\leqslant 70$, and pneumo-nia. It was demonstrated that intra- and extra-pulmonary insults result in SIRS developing to MODS, causing death.[5,16-18] Thus, doctors should be vigilant to identify early SIRS and take interventional measures. In this study, the survival rate of patients receiving early NCPAP respiratory support was as high as 77.78% (21/27); however, the mortality of patients having mechanical ventilation was as high as 63.16% (12/29) in patients in advanced phase or after NCPAP failure, indicating the importance of early intervention.[19-28] The mortality of patients in this study was 34.38%, and that of ARDS was 38.89%; both lower than those reported in adults, showing that children may have a better response to medical intervention than adults.[29-31]

Funding: This study was supported by a grant from Jiangxi Provincial Health Bureau of China (No. 010071).
Ethical approval: Not needed.
Competing interest: None declared.
Contributors: ZLQ proposed the study and wrote the first draft. CX analyzed the data. ZLQ is the guarantor.

References

1 Vasudevan A, Lodha R, Kabra SK. Acute lung injury and acute respiratory distress syndrome. Indian J Pediatr 2004;71:743-750.
2 Cheng IW, Matthay MA. Acute lung injury and the acute respiratory distress syndrome. Crit Care Clin 2003;19:693-712.
3 Spragg RG. Acute lung injury in 2003. Acta Pharmacol Sin 2003;24:1288-1291.
4 Wildins PA, Seahorn T. Acute respiratory distress syndrome. Vet Clin North Am Equine Pract 2004;20:253-273.
5 Brandstetter RD, Sharma KC, DellaBadia M, Cabreros LJ, Kabinoff GS. Adult respiratory distress syndrome: a disorder in need of improved outcome. Heart Lung 1997;26:3-13.
6 Yuan Z, Liu CF. Systemic inflammatory response syndrome in critically ill children and clinical application evaluation. Pediatr Emerg Med 2000;173-175.
7 Pediatric Critical Care Society of Chinese Medical Association. Diagnostic criteria for multiple system and organ failure of infants and children. Chin J Pediatr 1995;33:373.
8 Qiu HB, Chen DC, Liu DW, Jiang JM, Du B, Zhao CE, et al. Epidemiological analysis on acute respiratory distress syndrome. Natl Med J China 1997;77:785-787.
9 Neff MJ. The epidemiology and definition of the acute respiratory distress syndrome. Respir Care Clin N Am 2003;9:273-282.
10 Frutos-Vivar F, Nin N, Esteban A. Epidemiology of acute lung injury and acute respiratory distress syndrome. Curr Opin Crit Care 2004;10:1-6.
11 Flori HR, Glidden DV, Rutherford GW, Matthay MA. Pediatric acute lung injury: prospective evaluation of risk factors associated with mortality. Am J Respir Crit Care Med 2005;171:995-1001.
12 Zhu LQ, Zhang YQ. Clinical analysis on 15 cases of acute lung injury and acute respiratory distress syndrome. Chin J Pract Pediatr 1999;14:751-752.
13 Treggiari MM, Hudson LD, Martin DP, Weiss NS, Caldwell E, Rubenfeld G. Effect of acute lung injury and acute respiratory distress syndrome on outcome in critically ill trauma patients. Crit Care Med 2004;32:327-331.
14 Dobyns EM, Durmowicz AG, Henry DB, Loftness S, Stenmark KR. Current pediatric diagnosis and treatment. New York: Appleton & lange,1995;371-375.
15 Dellinger RP, Bone RC. To SIRS with love. Crit Care Med 1998;26:178.
16 Gando S, Kameue T, Matsuda N, Sawamura A, Hayskawa M, Kato H. Systemic inflammation and disseminated intravascular coagulation in early stage of ALI and ARDS: role of neutrophil and endothelial activation. Inflammation 2004;28:237-244.
17 He XL, Liu Z, Xia SY. Vascular endothelial injuries and changes of blood coagulation and fibrinolysis indexes in patients with acute respiratory distress syndrome. Chin Med Sci J 2004;19:252-256.
18 Odenstedt H, Aneman A, Karason S, Stenqvist O, Lundin S. Acute hemodynamic changes during lung recruitment in lavage and endotoxin-induced ALI. Intensive Care Med 2005;31:112-120.
19 Zhu LQ, Zhu YR, Wu X. Respiratory supports on acute lung

injury and acute respiratory distress syndrome. J Appl Clin Pedicatr 2000;15:57-58.
20 Esper AM, Martin GS. Evolution of treatments for patients with acute lung injury. Expert Opin Investig Drugs 2005;14:633-645.
21 Moran JL, Bersten AD, Solomon PJ. Meta-analysis of controlled trials of ventilator therapy in acute lung injury and acute respiratory distress syndrome: an alternative perspective. Intensive Care Med 2005;31:227-235.
22 Adhikari N, Burns KE, Mwade MO. Pharmacologic treatments for acute respiratory distress syndrome and acute lung injury: systematic review and meta-analysis. Treat Respir Med 2004;3:307-328.
23 Wu WS, Luo M, Yang CH. Comparison of lateral position and prone position ventilation in patients with acute lung injury/acute respiratory distress syndrome. Zhonghua Jie He He Hu Xi Za Zhi 2004;27:589-592.
24 Adhikari N, Burns KE, Meade MO. Pharmacologic therapies for adults with acute lung injury and acute respiratory distress syndrome. Cochrane Database Syst Rev 2004;(4):CD004477.
25 Kallet RH. Evidence-based management of acute lung injury and acute respiratory distress syndrome. Respir Care 2004;49:793-809.
26 Gattinoni L, Vagginelli F, Carlesso E, Taccone P, Conte V, Chiumello D, et al. Decrease in $PaCO_2$ with prone position is predictive of improved outcome in acute respiratory distress syndrome. Crit Care Med 2003;31:2727-2733.
27 Prodhan P, Noviski N. Pediatric acute hypoxemic respiratory failure: management of oxygenation. J Intensive Care Med 2004;19:140-153.
28 Han F, Jiang YY, Zheng JH, Hu Z, Gao ZC, He QY. Acute respiratory failure and noninvasive positive pressure ventilation treatment in patients with severe acute respiratory syndrome. Zhonghua Jie He He Hu Xi Za Zhi 2004;27:593-597.
29 Dahlem P, van valderen WM, Hamaker ME, Dijkgraaf MG, Bos AP. Incidence and short-term outcome of acute lung injury in mechanically ventilated children. Eur Respir J 2003;22:980-985.
30 Ware LB. Prognostic determinants of acute respiratory distress syndrome in adults: impact on clinical trial design. Crit Care Med 2005;33(Suppl 3):S217-222.
31 Matthay MA, Ware LB. Plasma protein C levels in patients with acute lung injury: prognostic significance. Crit Care Med 2004;32(Suppl 5):S229-232.

Received March 18, 2005
Accepted after revision May 10, 2005