นิพนธ์ต้นฉบับ

Adult respiratory distress syndrome in children

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Twenty-five children with adult respiratory distress syndrome (ARDS) who were admitted to pediatric intensive care unit (PICU) of Chulalongkorn Hospital during January 1987 to December 1991 were retrospectively reviewed. The incidence of ARDS in children without congenital heart diseases was 13.6: 1000 PICU admission with a mortality rate of 72%. Infections including pneumonia with sepsis (60%), shock from severe dengue hemorrhagic fever (12%) and septic shock in acute leukemia (12%) were the common predisposing causes followed by asphyxia from accidents and poisoning. Eighty four percent of the patients had complications during treatment and pulmonary hypertension was found in three survivors. There was no significant difference in age, sex, clinical and physiologic data and complications between the survivors and non-survivors except for longer duration of ventilatory support in the survivors.

Key words : *ARDS, Thai children.*

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ได้ทำการศึกษาถึงอุบัติการ สาเหตุ และผลการรักษาของกลุ่มอาการหายใจลำบากเช่นเดียวกับผู้ใหญ่ (Adult respiratory distress syndrome, ARDS) ในผู้ป่วยเด็กอายุ 3 เดือน -14 ปี ที่รับไว้รักษาในหอผู้ป่วยหนัก ของภาควิชากุมารเวชศาสตร์โรงพยาบาลจุฬาลงกรณ์ ในระหว่างเดือนมกราคม 2530-ธันวาคม 2534 พบว่ามีอุบัติการ 13.6 ต่อผู้ป่วยที่รับไว้รักษาในหอผู้ป่วยหนักทั้งหมด 1000 ราย โดยมีอัตราตายร้อยละ 72 สาเหตุของกลุ่มอาการนี้ส่วนใหญ่เกิดจากโรคติดเชื้อจากปอดอักเสบ (60%), ไข้เลือดออก (12%) และโลหิตเป็นพิษในผู้ป่วยมะเร็งเม็ดเลือดขาว (12%) ภาวะขาดออกซิเจนจากอุบัติเหตุและสารพิษเป็นสาเหตุที่สำคัญรองลงมา ร้อยละ 84 ของผู้ป่วยมีภาวะแทรกซ้อนขณะได้รับการรักษา สำหรับผู้ป่วยที่รอดชีวิตและติดตามการรักษาประจำพบว่ามีจำนวน 3 ราย ซึ่งมีความดันในปอดสูง จากการศึกษานี้ไม่พบความแตกต่างที่มีนัยสำคัญทางสถิติในเรื่องอายุ, เพศ, ลักษณะทางคลินิกและการเปลี่ยนแปลงทางสรีรวิทยา ตลอดจนภาวะแทรกซ้อนระหว่างกลุ่มที่รอดชีวิตและกลุ่มที่เสียชีวิต

Adult respiratory distress syndrome (ARDS) is a symptom complex characterized by dyspnea, tachypnea, cyanosis refractory to oxygen therapy, decreased lung compliance and diffuse alveolar infiltrates. It is the result of diffuse alveolar-capillary injury due to a variety of insults. It was first recognized in adults in 1967.[1] However, ARDS could be found in infants as early as 2 weeks of age.[2] After it had been firstly decribed in children by Holbrook et al in 1980,[3] other reports confirmed that ARDS could occur in infants and children with considerable mortality. Although modern technology which facilitated respiratory support could improve survival of the patients, ARDS remained one of the leading causes of acute respiratory failure in children with a high mortality rate (average 59%, range 28-95%).[2-5] Moreover, long term complications including pulmonary oxygen toxicity and abnormal pulmonary function were noted among survivors. Identification and effective management of predisposing causes are mandatory for prevention of severe ARDS and its complications. To our knowledge, the study on ARDS in Thai children has rarely been reported.[8] We, therefore, study the incidence, predisposing factors or underlying diseases, clinical course and outcome of ARDS in pediatric patients including analysis of possible factors affecting the outcome.

Materials and methods

All the patients who fulfilled the diagnostic criteria for ARDS and were admitted to the pediatric intensive care unit (PICU) of Chulalongkorn Hospital during January 1, 1987 to December 30, 1991 were retrospectively reviewed. Demographic data, predisposing causes, clinical course and outcome were analyzed to identify the differences between the survivors and non-survivors by using chi-square test, Fisher exact test and student-t-test where appropriate for statistical analysis. The factors with p-values < 0.05 were considered statistically significant.

The diagnostic criteria for ARDS in our study were[4,5]

1. previously normal lungs.
2. acute onset of respiratory distress within 48 to 72 hours of onset of severe illness or injury.
3. Severe hypoxemia : $P_aO_2 < 60$ mmHg while breathing greater than 60% supplemental oxygen.
4. poor lung compliance indicated by increased work of breathing (increased respiratory rate plus presence of retractions)
5. need for assisted ventilation for apnea, hypoxemia or hypercapnea
6. bilateral lung densities on the chest x-ray
7. exclusion of left heart disease and congestive heart failure.

Results

There were 25 patients who fulfilled the diagnostic criteria of ARDS admitted to PICU while total PICU admissions during the same period were 1826 cases. The calculated incidence of ARDS in our patients were 13.6 : 1000 PICU admissions. Eighteen patients died despite aggressive treatment. The mortality rate was 72%.

Demographic data : Of all the 25 patients, 13 were males and 12 were females (male : female ratio = 1.08 : 1). The age ranged from 3 months to 14 years with a mean age of 7.0 ± 5.1 years. There was no significant difference between the survivors and non survivors. (Table 1).

Table 1. Demographic data.

Causes	Non-survivors n = 18	Survivors n = 7
Age (years)		
X ± SD	6.9 ± 5.0	7.2 ± 5.3*
Sex		
male : female	10:8 (5:4)	3:4

Predisposing cause : Pneumonia with sepsis accounted for 60% of all the patients (Table 2). Among this group, staphylococcal pneumonia was the most common cause (4/15 cases). Measles and diphtheria with pneumonia were also infectious diseases associated with ARDS in 2 of our patients. Other significant predisposing causes were shock associated with dengue hemorrhagic fever (3/25 cases) and leukemia with neutropenia and sepsis. All patients with accidents and poisoning including car accident, cobra bite and near drowning had severe hypoxia due to respiratory arrest before admission. No statistically significant difference in predisposing causes between the survivors and non-survivors was observed.

Table 2. Predisposing causes.

Causes	Non-survivors (n = 18)	Survivors (n = 7)	Total (n = 25)
– Pneumonia + sepsis	11	4	15(60%)
– Dengue shock syndrome	1	2	3(12%)
– Acute leukemia + sepsis + shock	3	–	3(12%)
– Hydrocephalus + ICP*	1	–	1(4%)
– Car accident	–	1	1(4%)
– Cobra bite	1	–	1(4%)
– Near drowning	1	–	1(4%)

* ICP = increased intracranial pressure

Clinical and physiologic data : The onset of symptoms and signs of ARDS ranged from 5 hours to 3 days after admission with underlying or predisposing causes. The survivors tended to be recognized earlier than the non-survivors (26.0 ± 16.4 VS 41.9 ± 27.0 hours; Table 3). However, there was no statistically significant difference.

Table 3. Clinical and physiologic data.

	Non-survivors n = 18	Survivors n = 7
– onset (hrs.)		
X ± SD	41.9 ± 27.0	26.0 ± 16.4*
– approximate max. shunt (%)	30 ± 12	22 ± 10*
(range)	(10 – 41)	(10 – 32)
– max.PIP (cmH_2O)		
X ± SD	39.4 ± 16.6	42.5 ± 3.5*
(range)	(20 – 60)	(40 – 45)
– max.PEEP (CmH_2O)		
X ± SD	8.9 ± 4.3	11.5 ± 3.4*
(range)	(2-18)	(8-16)
– duration of ventilator therapy (days)		
X ± SD	7.3 ± 7.1	30.7 ± 25.7**
(range)	(0.12 – 26)	(10 – 63)

PIP = Peak inspiratory pressure
PEEP = Positive end expiratory pressure
* = no statistically significant difference ($P > 0.05$)
** = statistically significant difference ($P < 0.05$)

The approximated shunt was calculated by using modified Bergren's equation :

$$Qs/Qt = \frac{P(A-a)O_2 \times 0.003}{4.5 + P(A-a)O_2 \times 0.003} \times 100\%$$

Qs/Qt = intrapulmonary shunt
$P(A-a)O_2$ = alveolar-arterial oxygen tension difference

There was no significant difference between the survivors and non-survivors in their maximal shunt and ventilator settings to treat refractory hypoxemia in terms of peak inspiratory pressure and positive and expiratory pressure (PEEP). On the other hand, the survivors received longer duration of ventilator therapy (Table 3). The longest duration was 63 days in a child with car accident and pulmonary complications due to oxygen and positive pressure ventilation.

Complications : Gastro-intestinal (GI) bleeding and barotrauma (pneumothorax/ pneumomediastinum) were the two most common complications while pulmonary hemorrhage and multiple organ failure were the most fatal complications in our patients (Table 4).

Follow-up of the survivors : Three cases out of seven survivors were lost to follow up; all of them had pneumonia and sepsis as predisposing cause of ARDS. Among the four patients who were regularly followed-up for one year : three cases had pulmonary hypertension as detected by echocardiography, one of the two cases with dengue shock syndrome had pulmonary hypertension for 6 months. One patient with car accident developed congestive heart failure requiring drug therapy and one patient with acute leukemia had mild pulmonary hypertension.

Discussion

In our study, ARDS was an important cause of acute respiratory failure in children. The incidence of 13.6:1000 ICU admissions was comparable to previously reported rate of 8.5 to 10.4 cases : 1000 ICU admissions.[2-4,9-12] The varied incidence depended on the criteria used for diagnosis. However, Murray JF. et al had proposed acute lung injury scoring system to expand the definition of ARDS for early detection and prognosis of each patient.[13] We also used acute lung injury score together with conventional diagnostic criteria to make the diagnosis of ARDS by excluding all the patients with congenital heart diseases in order to abolish possible cardiac causes of respiratory distress or cardiogenic pulmonary edema. Therefore, the true incidence might be higher than reported.

Predisposing causes of ARDS in our pateints were not much different from the other previous reports.[2-4,8-12] Pneumonia with sepsis or septic shock ranked the most common cause among the previously normal and compromised hosts. Only one of the compromised host with ARDS in our study survived. Other causes of ARDS was asphyxia from various insults including accidents and poisoning. Of noted among the predisposing causes in our patients, hypovolemic shock from severe dengue hemorrhagic fever and cobra bite could cause ARDS in children. Since identification of clinical predispositions appeared to be the most practical and successful predictors of ARDS,[14] it was important for physicians to recognize the above mentioned predisposing causes and rendered early therapeutic interventions.

The main pathophysiologic changes in ARDS are permeability pulmonary edema from alveolo-capillary injury due to inflammatory mediators, proteolytic enzymes and toxic oxygen radicals released from macrophages and complement activations.[2,15-17] As a result, pre-existing surfactant is inactivated by high protein content in edematous fluid in the alveoli.[2,5,15] Surfactant production is also reduced due to type II pneumocytes damage leading to alveolar collapse and intrapulmonary shunt which is the main cause of refractory hypoxemia.[2,5,15-17] A recent retrospective study in children showed that high intrapulmonary shunt (> 50%) and alveolar-arterial oxygen tension difference ($P(A-a)O_2$ > 470 mmHg) were significant predictors of death in ARDS.[18] However, the physiologic data in our study could not demonstrate any differences between the survivors and non-survivors (Table 3) but the calculated intrapulmonary shunt was higher in those who died. Decreased lung compliance and increased airway resistance were the two major lung mechanic derangements in ARDS and should be monitored and carefully considered for effective ventilator therapy.[19] Although new modes of ventilation including inversed ratio ventilation (IRV) and high frequency ventilation (HFV) were reported to be a promising beneficial treatment of ARDS, positive end expiratory pressure (PEEP) with positive pressure ventilation remained the only proved effective ventilatory intervention.[20,21] High level of PEEP might be required to correct hypoxemia. As shown in our patients, those who survived received higher

level of PEEP despite having lower percentage of intrapulmonary shunt. However, there was no statistical significance which might be due to the small number of studied patients. The longer duration of ventilator therapy in the survivors was due to pulmonary complications after survival from the initial critical phase of acute respiratory failure.

More than eighty percent of our patients had complications during treatment (Table 4). Some patients had more than one complication. Gastro-intestinal bleeding and barotrauma which had been reported to be common complications of ARDS[21] were found in 20% of our patients. There was no difference in complications between the survivors and non survivors and non survivors. The overall mortality rate of 72% in our study was high but comparable to other studies.[2-4,8,18,21] Despite advances in patient care, technique and the presence of trained critical care pediatricians at tertiary centers, mortality rates in ARDS remained as high as 74%,[18] Further studies on predictors of ARDS leading to early treatment and prevention as well as althernative approach in addition to mechanical ventilation should be emphasized in order to reduce mortality and morbidity in pediatric patients.

Table 4. Complications.

Complications	Non-survivors n = 18	Survivors n = 7	Total case (%)
Barotrauma	2	3	5(20%)
G-I bleeding	3	2	5(20%)
Renal failure	2	2	4(16%)
Nosocomial pneumonia	1	1	2(8%)
Pulmonary hemorrhage	2	–	2(8%)
Liver failure	–	1	1(4%)
Multiple organs failure	1	–	1(4%)
SIADH*	1	–	1(4%)

NB : Each patient in each group may have more than 1 complication or no complication

* syndrome of inappropriate ADH secretion.

Conclusion

We presented a retrospective review of ARDS in 25 children without congenital heart diseases who were treated at the pediatric intensive care unit of Chulalongkorn Hospital during the past 5 years (1987-1991). The incidence, predisposing causes, mortality rate and complications were comparable to other reports. Our data could be a based-line information for further studies and added information on ARDS in Thai children which had been rarely reported.

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