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Organ-system injuries and risk factors related to mortality in neonates with severe birth asphyxia

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Abstract: **Objective** To analyze the effects of severe neonatal asphyxia on various organ-systems and to identify the risk factors associated with the resultant injuries and death. **Methods** The data of 170 cases in the last 10 years from January 1993 to March 2004 were analyzed. The risk factors associated with death were subjected to odds ratio (OR) analysis with the SAS software. **Results** There were 22 deaths in the 170 cases (12.5%). Organ-system injuries were evident in 165 of 170 cases (97.1%). In descending orders, the organ-system injuries were central nervous system [CNS, 66.5% (113/170)], pulmonary [62.9% (107/170)] and metabolic disorders [50.6% (86/170)]. The severity of injuries was in the reversed orders from metabolic disorders, pulmonary to CNS. From high risk to low, the factors which affected the mortality of severe asphyxia were, in order, severe CNS injury, ≥ 1 organ/system injury, respiratory failure, metabolic abnormality, electrolyte imbalance, blood-gas abnormality, pulmonary involvement, 10 min Apgar score ≤ 3 , gestational age < 37 weeks, hepatic involvement, cardiac involvement, raised PCO_2 , and hematologic involvement. **Conclusions** Organ-system injuries in addition to hypoxic-ischemic encephalopathy (HIE) were complications found in the majority of the cases with severe neonatal asphyxia. The risk factors such as CNS injury or HIE, pulmonary dysfunction and failure, and multiorgan dysfunction syndrome (MODS) involving more than three organ-systems should be detected and recognized early so that early intervention can be instituted to reduce the mortality.

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Key words: Asphyxia; Organ-system injuries; Risk factors; Infant, newborn

新生儿重度窒息器官损害及死亡危险因素分析

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【摘要】 目的 回顾性分析我院170例新生儿重度窒息的临床情况及各脏器受累损伤程度, 了解与死亡有关的危险因素。方法 对1993~2004年我院NICU收治的重度窒息新生儿170例资料进行分析, 用SAS软件对与死亡有关危险因素进行OR分析。结果 170例中死亡22例(12.5%), 165例(97.1%)出现各脏器的并发症, 各脏器受累机会的次序依次为中枢神经系统, 肺, 代谢系统等; 严重程度依次为代谢, 肺, 中枢神经系统等。与死亡有关的危险因素依次为中枢神经系统严重受累, 1个以上脏器严重受损, 呼吸衰竭, 代谢紊乱, 电解质紊乱, 血气异常, 肺损害, 10分钟Apgar评分 ≤ 3 , 胎龄 < 37 周, 肝脏损害, 心脏损害, PCO_2 增高和血液系统损伤。结论 器官/系统损害是除HIE外新生儿重度窒息的主要并发症, 严重威胁生命并且可以导致死亡; 对于一些造成死亡的危险因素应该引起重视和早期干预。

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【关键词】 窒息; 器官损害; 危险因素; 新生儿

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Neonatal asphyxia often causes multiple organ and system injuries. The common organs involved are the kidneys, brain and lungs. Ischemic damage to these organs accounts for one-third mortality in born alive newborns, and results in severe neurodevelopmental sequelae among the survivors. The objectives of this study were to analyze and identify the damage to diffe-

rent organs and systems caused by severe neonatal asphyxia and to identify the risk factors for death.

Subjects and methods

Subjects

One hundred and seventy neonates with severe as-

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phyxia admitted between January 1993 and March 2004 were included in this study. Severe asphyxia was defined according to the Apgar scores at 1 and 5 minutes^[1].

Methods

Retrospective data from 170 cases were collected. The following parameters were included in the database and subsequent analysis: gestational age (GA), birth weight (BW), Apgar scores at 1, 5 and 10 minutes, place of delivery, physical signs of various organ-

system injuries, and laboratory investigations on admission day, such as blood-gas analysis, serum electrolytes and glucose, renal and liver function tests, cranial ultrasound, computerized tomography (CT), electroencephalogram (EEG), and echocardiography (ECHO). Indices of organ-system injury and their severity are shown in Table 1 according to published literatures^[2-3]. The outcomes of the 170 cases were divided into deaths and survivors.

Table 1 Indices of organ-system injury and their severity

	Mild to moderate	Severe
CNS	HIE I to II, IVH I to II,	HIE III, IVH III to IV
Pulmonary	Respiratory failure type I	Respiratory failure type II
Cardiac	Arrhythmia, ST-T changes by ECG; CK-MB mildly raised	Heart failure
Renal	BUN > 7.1 but < 15 mmol/L; Cr > 4 but < 133 μ mol/L	BUN > 15 mmol/L; Cr > 133 μ mol/L
Hepatic	GPT > 40 U/L	GPT > 80 U/L
GI	Gastric and abdominal distention; Mild vomiting	GI paralysis and ulcer; Severe GI distention
Blood	Prolonged PT < 2 sec; PLT < 100×10^9 /L; Mild to moderate anemia	DIC
Metabolism	pH: 7.2-7.3; BE: -6 to -12; Serum glucose 20-30 mg/dL;	pH: < 7.2; BE: -12 mmol/L and above; Serum glucose < 20mg/dL
SerumElectrolytes	Na < 130 or > 150 mmol/L; K < 3.5 or > 5.5 to 7 mmol/L	Na < 110 or > 160 mmol/L; K < 2.5 or > 7 mmol/L

CNS: central nervous system; HIE: hypoxic-ischemic encephalopathy; IVH: intraventricular hemorrhage; GPT: glutamate-pyruvate transaminase; GI: Gastro-intestinal; PT: prothrombin time; PLT: blood platelets count; DIC: disseminated intravascular coagulation; BE: base excess

Statistical analysis

Statistical analysis was conducted with SAS statistical software. The variances were described as $\bar{x} \pm s$. The differences between groups were analyzed by *t* test before which homogeneity of the variances was tested. The odds ratio (OR) and its 95% confidence interval (CI) were calculated. The significance of OR based on X^2_{MH} was analyzed.

Results

Clinical data

There were 114 boys and 56 girls. Their gestational ages ranged from 27⁺⁵ weeks to 43⁺³ weeks (mean 37.9 \pm 3.2 weeks). Forty-four infants were preterm (25.9%), 129 term (71.2%) and 5 post-term (2.9%). Sixteen infants (9.4%) were delivered in Shanghai Xinhua Hospital and the remaining 154 (90.6%) were delivered at home or in other hospitals. The birth weight (BW) ranged from 690 g to 4 000 g (mean 2 638 \pm 879 g). One hundred and forty (82.5%) cases had an Apgar score below 3 at 1

minute and 69 (40.6%) had an Apgar score below 3 at 5 minutes. These included 28 cases whose Apgar scores were below 3 at 5 minutes, although the scores were higher than 3 at 1 minute. Fourteen (8.2%) cases had Apgar scores remained below 3 at 10 minutes. One hundred and forty-eighty (87.5%) neonates survived and 22 (12.5%) died.

Organ-system injuries in patients with severe asphyxia

Of the 170 cases, 165 (97.1%) had evidence of organ-system involvement. CNS was the commonest organ involved in severe asphyxia, followed by pulmonary and metabolic system. Relatively fewer cases had involvements of heart, kidneys, gastrointestinal tract, as well as hematological system and electrolytes balance. At the same time the most severe injuries involved the CNS and pulmonary (Table 2).

One organ-system was affected in 17 cases, 2 in 36 cases, 3 in 42 cases, 4 in 30 cases, 5 in 17 cases, 6 in 11 cases, 7 in 9 cases, 8 in 2 cases, and 9 in 1 case. Mild injuries occurred in 79 cases (46.5%) and severe injuries in 86 cases (50.6%).

Table 2 Organ-system injuries in patients with severe asphyxia

	CNS	Pulmonary	Cardiac	Renal	Hepatic	GI	Blood	Metabolic	Electrolytes
Not affected	57(33.5%)	63(37.1%)	103(60.6%)	134(78.8%)	146(85.9%)	145(85.3%)	147(86.5%)	84(49.4%)	147(90.2%)
Affected	113(66.5%)	107(62.9%)	67(39.4%)	36(21.2%)	24(14.1%)	25(14.7%)	23(13.5%)	86(50.6%)	16(9.8%)
Severe	24(14.1%)	25(14.7%)	4(2.4%)	20(11.8%)	12(7.1%)	6(3.5%)	5(2.9%)	44(25.8%)	2(1.2%)

Risk factors related to mortality of neonates with asphyxia

From high risk to low, the factors which affected the mortality of severe asphyxia were, in order, severe CNS injury, ≥ 1 organ/system injury, respiratory failure, metabolic abnormality, electrolyte imbalance, blood-gas abnormality, pulmonary involvement, 10 min Apgar ≤ 3 , GA < 37 weeks, hepatic involvement, cardiac involvement, raised PCO₂, and hematologic involvement (Table 3). Some factors such as the severity of organ/system injury and the birth place of infants were not significantly associated with death and they were not listed.

Table 3 Risk factors related to mortality of neonates with asphyxia

Injuries	OR	95% CI	χ^2	P
Severe CNS injury	33.1	13.7, 79.9	60.562	<0.01
Injured organ-system ≥ 1	26.8	6.4, 112.4	20.231	<0.001
Respiratory failure	9.6	3.9, 23.2	24.948	<0.001
Metabolic abnormality	7.8	3.1, 18.0	20.468	<0.001
Electrolyte imbalance	6.4	2.1, 19.9	10.476	<0.01
Blood-gas abnormality	4.7	1.6, 14.1	7.646	<0.01
Pulmonary injury	4.7	1.5, 15.1	6.710	<0.05
10 min Apgar ≤ 3	4.4	1.5, 14.0	6.981	<0.01
GA < 37 weeks	4.4	1.8, 10.5	10.759	<0.01
Hepatic injury	3.6	1.3, 10.0	6.492	<0.05
Cardiac injury	3.1	1.3, 7.7	6.174	<0.05
Raised PCO ₂	2.9	1.1, 7.81	4.443	<0.05
Hematologic injury	2.9	1.01, 8.11	4.056	<0.05

Discussion

Asphyxia at birth is a major cause of acute organ-system injury or multiorgan dysfunction syndrome (MODS) in neonates^[4]. In this retrospective study of 170 newborns with severe asphyxia, 97.1% of them had such complications. In descending orders, the organ-system injuries were CNS, pulmonary and metabolic disorders. The severity of injuries was in the reversed orders from metabolic disorders, pulmonary to CNS. This was probably due to the differences in the susceptibility of organ-system as well as the effects of redistribution of blood supply to various organs during the asphyxial process^[5-6]. Metabolic disturbances were the results of impairment in functions of organ-systems. Meanwhile some important organ-systems such as the heart appeared to be less involved, and also less severe even when involved. This could be due to the possibility that the heart was protected to a certain extent during hypoxia and ischemia. However, this may also possibly due to the fact that routine clinical investigations for cardiac injury were inadequate or that investi-

gations were not performed timely enough.

MODS frequently occurred during the acute stage of the neonatal asphyxia. In this study it occurred in 87% of the cases, and in 40% of the cases more than 3 organ-systems were involved. There are serious implications for the clinicians in terms of interventions. To avoid the severe MODS, anticipatory organ-system based monitoring and early detection for systematic disorders must be instituted. Some studies have shown that all infants with severe post-asphyxial encephalopathy or HIE had evidence of dysfunction of at least one organ/system in addition to the central nervous system^[7]. This conforms with the criteria of the American College of Obstetricians and Gynecologists^[8] but not with some published reports of organ/system dysfunction in neonates with asphyxia of variable severity^[9]. There may be two reasons for the variability in the reported incidence of MODS. Firstly, by the selection criteria for the studies of MODS; at the mild end of the spectrum are cases of "intrapartum asphyxia" with or without HIE during the neonatal period, and at the severe end of the spectrum are known cases of cerebral palsy attributed to intrapartum asphyxia. Secondly, the differences in the definition of MODS with respect to the number of organs included in its definition, the definition of "organ/system" (for example, kidneys, hypocalcaemia), and the definition of dysfunction of each organ/system^[4].

CNS impairment or HIE was the most significant risk factor leading to death in this study. This was also consistent with other studies^[2,3,5]. Pulmonary injury and its functional failure was the second most significant risk factor associated with death. This was not always shown in other studies and not highlighted as an important predictor in prognosis^[10]. This may be due to different methods used in the investigation of risk factors, or it was not included in the definition of MODS. Apgar score of less than 3 for a prolonged duration, especially when it remained less than 3 at 10 minutes was consistently shown to be a risk factor associated with death in this study. Premature, metabolic disorders including blood-gas abnormalities and severe MODS were other risk factors associated with death.

In conclusion, organ-system injuries and MODS in addition to HIE are complications found in the majority of cases with neonatal asphyxia. Risk factors such as CNS injury or HIE, pulmonary dysfunction and failure, MODS, and low Apgar scores at 5 to 10 minutes are significantly associated with death.

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(Edited by Le ZHONG)

· 消息 ·

2006 年全国儿科热点研讨会征文通知 (第一轮通知)

由中国当代儿科杂志社和全军儿科学会联合举办的“全国儿科热点研讨会”拟定于2006年4月中旬在杭州市召开,大会将采取专家讲座和大会交流相结合的形式。专家讲座热点内容有:①新生儿(用氧、感染与抗生素应用);②遗传代谢与神经病(小儿遗传代谢病诊治、PKU研究近况与串联质谱仪、遗传代谢病相关癫痫、小儿头颅CT与MRI);③风湿与免疫(川崎病和JRA诊治近况、免疫缺陷病、骁悉的临床应用);④临床科研(循证医学与医学伦理、临床研究设计与医学统计、医学论文写作中常见问题)。拟参加讲课的专家有杨锡强、吴希如、何晓琥、桂永洁、魏克伦、何乃强、蔡方成、王慕逖、罗小平、顾学范、杨艳玲等。现征集会议论文,主要内容为儿科及新生儿疾病的基础与临床研究,临床诊断与治疗体会。要求为未公开发表过的学术论文摘要,500字左右(包括目的、方法、结果、结论)。被录用的论文将编入“会议论文集”,其中优秀的稿件可在中国当代儿科杂志上发表。稿件上请注明作者姓名、单位、邮编、电话、传真。推荐Email投稿,“主题”请写“会议征文”。亦接受邮寄投稿,请在信封上注明“会议征文”。无需寄审稿费。无论文者亦欢迎参加会议。

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