Incidence of brain injuries in premature infants with gestational age ≤34 weeks in ten urban hospitals in China

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Background: There is a large number (1.5 million per year) of premature births in China. It is necessary to obtain the authentic incidences of intraventricular hemorrhage (IVH) and periventricular leukomalacia (PVL), the common brain injuries, in Chinese premature infants. The present multicenter study aimed to investigate the incidence of brain injuries in premature infants in ten urban hospitals in China.

Methods: The research proposal was designed by the Subspecialty Group of Neonatology of Pediatric Society of the Chinese Medical Association. Ten large-scale urban hospitals voluntarily joined the multicenter investigation. All premature infants with a gestational age ≤34 weeks in the ten hospitals were subjected to routine cranial ultrasound within three days after birth, and then to repeated ultrasound every 3-7 days till their discharge from the hospital from January 2005 to August 2006. A uniform data collection sheet was designed to record cases of brain injuries.

Results: The incidences of overall IVH and severe IVH were 19.7% (305/1551) and 4.6% (72/1551), respectively with 18.4% (56/305) for grade 1, 58.0% (177/305) for grade 2, 17.7% (54/305) for grade 3 and 5.9% (18/305) for grade 4 in nine hospitals. The incidences of overall PVL and cystic PVL were 5.0% (89/1792) and 0.8% (14/1792) respectively, with 84.3% (75/89) for grade 1, 13.5% (12/89) for grade 2, and 2.2% (2/89) for grade 3 in the ten hospitals. The statistically significant risk factors that might aggravate the severity of IVH were vaginal delivery (OR=1.883, 95% CI: 1.099-3.228, \(P=0.020\)) and mechanical ventilation (OR=4.150, 95% CI: 2.384-7.223, \(P=0.000\)). The risk factors that might result in the development of cystic PVL was vaginal delivery (OR=21.094, 95% CI: 2.650-167.895, \(P=0.000\)).

Conclusions: The investigative report can basically reflect the incidence of brain injuries in premature infants in major big cities of China. Since more than 60% of the Chinese population live in the rural areas of China, it is expected to undertake a further multicenter investigation covering the rural areas in the future.


Key words: incidence; intraventricular hemorrhage; multicenter investigation; periventricular leukomalacia; premature infants

Introduction

Intraventricular hemorrhage (IVH) and periventricular leukomalacia (PVL), the common brain injuries in premature infants, are major causes for early death in the neonatal period and later motor and cognitive disabilities. Post-hemorrhagic...
hydrocephalus and periventricular hemorrhagic infarction are major complications of IVH. PVL is an intractable brain injury in premature infants, pathologically characterized by focal necrosis and diffuse injury. Ischemia and infection are believed to be the main pathogenic factors for PVL in premature infants. Especially, the peroxynitrite generated from lipopolysaccharide-activated microglia mediates the destruction of pre-oligodendrocytes (preOLs). Either by periventricular hemorrhagic infarction following IVH or PVL induced by ischemia or infection, hypomyelination takes place finally because of a damage or loss of preOLs, leading to the sequelae of cerebral palsy and mental retardation.

In consideration of the higher absolute number (1.5 million per year) of premature births in China and the severity of brain injuries in premature infants, a multicenter investigation for brain injuries in premature infants was conducted in China by the Subspecialty Group of the Neonatology of Pediatric Society, the Chinese Medical Association. This report describes the incidences of brain injuries (IVH and PVL) in premature infants with ≤34 weeks of gestational age in ten large-scale urban hospitals in China.

### Methods

#### Participating hospitals

Ten large-scale urban hospitals that were the biggest hospitals at provincial level and all belonged to the Third Class and A Level (the highest level) in China participated in the multicenter investigation. Nine hospitals were involved in investigations of IVH and PVL incidences, and one hospital was only investigated for PVL incidence. Permission for the study was obtained from the human research committees of the participating hospitals, and informed consent was obtained from the relatives of the infants enrolled in this study.

#### Subjects and study course

Premature infants with the gestational age of ≤34 weeks were investigated from January 2005 to August 2006. Malformed premature infants were excluded.

### Methods

#### Research proposal

The research proposal was drafted by the Subspecialty Group of Neonatology of the Pediatric Society, the Chinese Medical Association. The proposal was discussed and amended by famous neonatologists in the field of neonatal brain injuries in China. A uniform sheet for data collection was designed for recording cases of brain injuries.

#### Cranial ultrasound scan

An initial bedside real-time cranial sonography was performed by radiologists for all premature infants from the ten hospitals within 3-7 days of birth. Most infants had one or more follow-up examinations at intervals varying from every other day to weekly until discharge. IVH was graded 1 to 4 according to the system of Papile et al., and grades 3 and 4 were considered "severe" IVH. Post-hemorrhagic hydrocephalus was diagnosed when there was progressive ventricular dilation on sonography. PVL was graded 1 to 4 according to the classification of de Vries et al., and grade II and above was defined as cystic PVL, a more severe pathological type.

#### Statistical analysis

All data were taken from the records and entered into Foxpro software for analyses. Statistical analysis was made with Student's *t* test (unpaired), the chi-square test, and odds ratio with SPSS 11.5 software. Differences between the groups were considered statistically significant when *P*<0.05.

### Results

#### General clinical data

Totally 1792 premature infants with ≤34 weeks of gestational age were enrolled for investigating the incidence of brain injuries. Of whom, 1551 were admitted to the nine hospitals that participated in the investigation of IVH incidence. IVH was found in 305 infants. Their average gestational age was 31.7±2.2 weeks (n=303, range: 27.0-34 weeks), and birth weight was 1751.1±462.7 g (n=305, range: 860-2500 g). The ratio of male to female of the premature infants was 2.3:1. Forty-two infants were outborn. The Apgar score was 7.8±2.4 (n=228, range: 1-10) at one minute, including 18 infants with Apgar score ≤3; 9.0±1.7 (n=228, range: 1-10) at five minutes, including 5 infants with Apgar score ≤3. Vaginal delivery was taken in 149 infants, cesarean birth in 153, and forceps delivery in 3.

Altogether 1792 premature infants were admitted to the ten hospitals participating in the investigation of PVL incidence, and PVL was diagnosed in 89 infants. Their average gestational age was 32.0±1.9 weeks (n=87, range: 26.6-34 weeks), and birth weight was 1810.8±449.1 g (n=89, range: 960-2300 g). The ratio of male to female in the premature infants was 2.3:1. There were 15 outborn infants. The Apgar score was 7.8±2.4 (n=80, range: 1-10) at one minute, and 6 infants had an Apgar score ≤3. The Apgar score was 9.0±1.6