Neurodevelopmental Outcome of Infants and Children with Acute Meningitis/ Encephalitis/Encephalopathy

Thesis

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بسم الله الرحمن الرحيم

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم الحكيم

صدق الله العظيم

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Doaa Abdelhakam

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List of Abbreviations

Abbrev.	Full-term
AAP	: American Academy of Pediatrics
AB	: Adaptive behavior
ADEM	: Acute disseminated encephalomyelitis
ADS	: Acute demyelinating syndromes
AEE	: Acute encephalitis/encephalopathy
AMPA	: α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid
ANOVA	: A one-way analysis of variance
BMS	: Bacterial meningitis score
CMV	: Cytomegalovirus
CNS	: Central nervous system
CPCCRN	: Collaborative Critical Care Research Network
CSF	: Cerebrospinal fluid; ANC, absolute neutrophil count
CT	: Computed tomography
ER	: Emergency room
FSS	: Functional Status Scale
GABAB	: γ-aminobutyric acid-B
GBS	: Group B streptococcus
GFAP	: Glial fibrillary acidic protein
HIV	: Human immunodeficiency virus
HSE	: Herpes simplex encephalitis
HSV	: Herpes simplex virus
IBAS	: Independent Behavior Assessment Scale
ICP	: Increased intracranial pressure
IQ	: Intelligence quotient

IV	: Intravenous
LA	: Latex agglutination
LP	: Lumbar puncture
MS	: Multiple sclerosis
NMDA	: N-methyl-D-aspartate
PCPC	: Pediatric Cerebral Performance Category
PICU	: Pediatric intensive care unit
POPC	: Pediatric Overall Performance Category
ROC	: Receiver operating characteristic curve
SAH	: Subarachnoid hemorrhage
SB5	: Stanford-Binet Intelligence Scales – Fifth Edition
SD	: Standard deviation
SDE	: Subdural empyema
SIADH	: Syndrome of inappropriate secretion of the antidiuretic hormone
SPSS	: Statistical Program for Social Science
TB	: Tuberculosis
TBM	: Tuberculous meningitis
VGKC	: Voltage-gated potassium channel

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ABSTRACT

Background: Acute encephalitis/encephalopathy (AEE) is a devastating cause of severe neurodevelopmental sequelae or death in children. Morbidity assessments are becoming a more important aspect of pediatric outcomes research especially in studies with a significant risk for decreased functional status due to neurologic processes. **Aim of the Study:** Correlate clinical, laboratory, radiological and electro-physiological parameters to short term neuro-developmental outcome in infants and children presenting with acute encephalitis/encephalopathy. **Subjects and Methods:** After approved by pediatric council, faculty of medicine (Ain Shams University), this prospective case-control study was conducted at ER, neurodevolpmental clinic. Children's Hospital, Faculty of Medicine, Ain Shams University during the period from June, 2016 till august, 2017of 15 months time frame. All the steps were explained to the care givers in details, verbal acceptance was taken from the participants in the study. **Conclusion:** CNS infection in infant and children causes variable degrees of disabilities and high rates of sequelae among survivors. **Recommendations:** Neurodevelopmental assessment during follow-up of patients with CNS infection is critical to our understanding of the burden of the adverse consequences of the disease. Bayley scales III edition scoring system should be involved in evaluation of patients with CNS infection.

Key words: neurodevelopmental outcome, infants, children, acute meningitis, encephalitis, encephalopathy, CNS infections

Introduction

Acute encephalitis/encephalopathy (AEE) is a devastating cause of severe neurodevelopmental sequelae or death in children ***(Tsukahara et al., 2013).***

Outcome studies of acute neurological compromise are expanding their focus beyond mortality to include functional status, quality of life, and other outcomes ***(Ebrahim et al., 2013, Coleman et al., 2012, Rennick et al., 2011, Taylor et al., 2003, Knoester el al., 2008).***

Morbidity assessments are becoming a more important aspect of pediatric outcomes research especially in studies with a significant risk for decreased functional status due to neurologic processes ***(Pollack et al., 2014).***

Assessing ongoing brain injury and predicting outcomes is expected to be extremely valuable in children presenting with AEE ***(Tsukahara et al., 2013).*** The previous group of authors studied three groups of children; group 1 included 27 children served as control who didn't have AEE, group 2 included 13 children with normal resolution after the AEE, and group 3 included 10 children who developed severe sequelae or death. In the early CSF samples of the included AEE participants, 3 brain injury markers were measured; S-100B, glial fibrillary acidic protein (GFAP) and tau protein. The results showed that

all brain injury markers were significantly higher in group 3 compared to group 1 and 2. Also they found that S-100B was significantly higher in non-survivors than in survivors. They concluded that combined measurement of brain injury markers show promise as predictors of clinical outcomes in children with AEE.

In a recent interesting research done by ***Nishiyama et al. in (2016)***, they recruited children admitted to the pediatric intensive care unit (PICU) because of convulsions or impaired consciousness with fever between 2002 and 2013. They included only those with no neurological abnormalities before the onset. They assessed outcomes using the Pediatric Cerebral Performance Category (PCPC) scale, with a score of 1 representing normal performance; 2 mild disability; 3, moderate disability; 4, severe disability, 5 vegetative state and 6 brain death. Seventy eight children were included with 20 months median age. Fifty one scored 1 on the PCPC, 13 scored 2, 3 scored 3, 5 scored 4, one scored 5 and 5 scored 6 at discharge. Whereas seven of the 13 cases who scored a 2 on the PCPC recovered normal brain function after 12 months, none of the nine cases that scored a 3-5 on the PCPC recovered normal function. They concluded that moderate to severe disability caused by acute encephalopathy had lasting consequences on brain function, whereas mild disability might result in improved function.

Still tackling outcomes of encephalopathy/encephalitis in children, a multitude of Japanese papers are in the field**.** ***Kawano et al. (2011)*** aimed in their retrospective observational study at investigating the clinical variables and therapeutic options associated with the outcome of children with AEE. They explored the relationships between the clinical information at admission and neurological outcome evaluated using PCPC at 12 months after admission in 43 patients treated at different Japanese PICUs. Applying multivariate analysis, younger ages and elevated serum lactate dehydrogenase were associated with adverse outcomes, whereas early initiation of cooling was related to favorable outcomes. For normothermic children PCPC scores were dependent on the CT findings suggestive of brain edema, serum LD levels and Glasgow Coma Scale at admission. For hypothermic children, PCPC scores depended on longer delay in cooling initiation. They concluded that without therapeutic hypothermia, the outcome of children was determined by variables suggestive of the severity of encephalopathy/encephalitis at admission. Hypothermia may have pivotal impacts on the outcome of children according to the timing of cooling initiation following AEE.

Several methods are present for assessing general functional status. The Pediatric Overall Performance Category (POPC) and the Pediatric Cerebral Performance Category

scales) which are qualitative assessments of performance based on the Glasgow Outcome Scale ***(Fiser 1992 and Fiser et al., 2000).*** More recently, the Collaborative Critical Care Research Network (CPCCRN) developmented and validated the Functional Status Scale (FSS), which has the potential advantages of increased objectivity, increased granularity, and greater quantification compared with the POPC/PCPC system ***(Pollack, 2009).***

Aim of the Study

Correlate clinical, laboratory, radiological and electro-physiological parameters to short term neuro-developmental outcome in infants and children presenting with acute encephalitis/encephalopathy.