Neonatal Epilepsy

"Essay"
Submitted for fulfillment of the requirements of M.Sc.degree in pediatrics

by
Dina Hossam El Din Hamed M.B.,B.Ch
Faculty of Medicine
Cairo University

supervised by

Prof. Dr. Zahraa Mohamed Ezz El Din
Prof. Of Pediatrics
Faculty of Medicine
Cairo University

Dr. Ranya Aly Hegazy
Lecturer of Pediatrics
Faculty of Medicine
Cairo University

Dr. Yasmine Amr Mansy
Lecturer of Pediatrics
Faculty of Medicine
Cairo University

Faculty of Medicine
Cairo University
2007

ACKOWLEDGEMENT

First of all, I would like to thank ***Allah*** the merciful and compassionate for making all this work possible and for everything that I have and everything I will ever be.

I have been honored and privileged to have worked under the supervision of such distinguished and great professors that many people would dream of having such a chance.

I would like to express my deepest gratitude to ***Prof. Zahraa Mohamed Ezz El Din***, Professor of neonatology, Cairo University, for her unlimited support, valuable supervision and kind guidance. I thank her beyond words can convey. I hope I will be able to follow her footsteps.

I am deeply indebted to ***Dr. Ranya Aly Hegazy***, she has been there for me from the beginning with her exceptional assistance, outstanding devotion, valuable time, enthusiastic encouragement and sincere guidance.

Words can not express my deep appreciation for ***Dr. Yasmine Amr Mansy***. I m very thankful to her for her continuous support, and correction. I will always owe her so much.

Furthermore, I would like to convey my special thanks to all *the Staff members* in the Pediatric Hospital of Cairo University who taught me the true meaning behind being a doctor, and to *my dear colleagues* for their kind support.

SPECIAL DEDICATION

Last but not least I am deeply indebted to *my family (my father, my mother, my husband and my daughters "Mariam and Malak")* who were always there for me with their endless support and encouragement, they have always had faith in me. In fact I owe them everything that I am. To them I dedicate my work and to them I say **THANK YOU**

Abstract

Epilepsy is a serious brain disorder.

Neonatal seizures fo not reprseent a homogeneous clinical entity and it can be difficult to distnguish epileptic from non-epileptic seizures when ictal semiolog is not EEG related.

Neonatal seizures are difficult detect, diagnose, and manage.

Treatment of sizures involves identifying and treating the underlying etiology of the seizure and appropriate use of pharmacologic interventions.

Key Words:

Neonatal seizures, Epilepsy.

CONTENTS

Page

List of Tables

Tables *Page*

List of Figures

Figures *Page*

List of abbreviations

AEDs: Antiepileptic drugs

ACh : acetylcholine

aEEG: Amplitude-integrated electroencephalogram

AMPA: α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid

BFNC: Benign familial neonatal convulsions

BFN/IS: Benign familial neonatal infantile seizures

BINC: Benign infantile neonatal convulsions

Ca: Calcium

CBC: Complete blood count

CFM: Cerebral function monitor

CL: Chloride

CNS: Central nervous system

CRH: Corticotropinreleasing hormone

CT: Computed tomography

EAA: Excitatory amino acid

ECD : Electroclinical disassociation

ECl: Cl- equilibrium potential

EEG: Electroencephalogram

EIEE: Early infantile epileptic encephalopathy

EME: Early myoclonic encephalopathy

EMG: Electromyography

FT: Full term

GABA: Gamma amino butyric acid

GABA-R: GABA receptors

GEFS+: Generalized epilepsy with febrile seizures plus

GLU-R: Glutamate receptors

ICEGTCS: Intractable childhood epilepsy with tonic-clonic seizures

ILAE: International league against epilepsy

IM: Intramuscular

IS :Infantile spasm

IV: Intravenous

K: Potassium

MRI: Magnetic resonance imaging

MCD: Malformations of cortical development

Na: Sodium

NAA: N-acetylaspartate

NKCC1: Na+,K+,2Cl− cotransporter

NMDA: *N*-methyl-D-aspartate

NS: Neonatal seizures

PN: Postnatal day

PT: Preterm

SMEI: severe myoclonic epilepsy of infancy

SNR: Substantia nigra pars reticulata

Review of Literature

INTRODUCTION

Epilepsy is a serious brain disorder characterized by recurrent unprovoked seizures. Seizures are the most common neurological emergency in newborns ***(Rennie and Boylan, 2003)***. The incidence of seizures in the neonatal period is greater than in any other time of life with most seizures occurring within the first week of life ***(Granelli and Mcgrath, 2004).*** The incidence of seizures in infants born at term is 1.5 - 3.0 per 1000 live births; the incidence is even higher in preterm infants, ranging from 50 - 150 per 1000 live births. These figures are probably underestimations as these figures only include clinical and electroclinical seizures. The exact incidence of electroencephalographic, clinically silent seizures is as yet unknown***(Volpe, 2001)***.

A significant percentage of neonatal seizures (NS), however, are symptoms of severe or progressive brain disease and prelude to development of neurological deterioration and epilepsy. Therefore, NS do not represent a homogeneous clinical entity and it can be difficult to distinguish epileptic from non-epileptic seizures when ictal semiology is not EEG related***(Mastrangelo et al., 2005).***

Seizures are the most frequent clinical sign of neurological dysfunction in the neonate***(Volpe, 2001).*** Depending on the immaturity of the brain, seizures may disrupt the processes of cell growth, division, migration, myelination, receptor formation, and stability of the synapse, thus contributing to the neurological sequelae***(Scher, 2003)***. The majority are occasional seizures, occurring as reactive events to acute insults, systemic diseases or disturbances, and subsiding soon after removal of the causative event***(Mastrangelo et al., 2005).***

Neonatal seizures are rarely idiopathic, therefore an extensive diagnostic workup is needed to establish the cause of seizures in newborn period***(Malik et al., 2003).*** Most seizures are triggered by acute illness such as hypoxic ischemic encephalopathy, stroke, or infection; rarely are they triggered by epilepsy per se***(Clancy, 2006).*** Determination of aetiology is highly critical because it affords the opportunity to treat specifically and also to make a meaningful prognostic statement***(Patrizi et al., 2003).***

Neonatal seizures(NS) are markers for time specific aetiologies during antepartum, intrapartum and neonatal time periods. Seizures with or without encephalopathic signs can represent a continuum of maternal, placental, fetal and neonatal risk factors and disease states***(Scher, 2006).***

The 1989 ILAE (international league against epilepsy) classification of epilepsy and epileptic syndromes was found unsatisfactory in newborns***(Arzimanoglou and Aicardi, 2001).*** According to it, most of NS were classified under epilepsies and syndromes undetermined whether focal or generalized, with the exception of four rare but well defined electro-clinical syndromes: early myoclonic encephalopathy (EME), early infantile epileptic encephalopathy (EIEE), benign idiopathic neonatal convulsions (BINC), benign familial neonatal convulsions (BFNC). The 2001 ILAE proposed diagnostic scheme for neonates with epileptic seizures and with epilepsy which offers a variety of approaches to classification increasing its power to characterize individual patients in a less ambiguous manner with clear etiologic, therapeutic and prognostic implications***(Engel , 2001).***

Clinical experience suggests two major components to the relationship between brain development and epilepsy. First, the maturational state of the immature brain appears to generally decrease seizure threshold and to contribute to a different seizure phenotype from the adult brain. Second, certain forms of seizures, when present during development, may modify brain maturation, resulting in chronic epilepsy and or neurocognitive deficits***(Jensen, 1999).***

The first studies that reported on outcome of neonatal seizures showed a 20% incidence of evolution into epilepsy. When EEG monitoring was added to the clinical data, the rate of seizures predictive of epilepsy rose to 56%***(Pisani et al., 2004).*** Neonates with a suboptimal Apgar score (5-minute Apgar Score less than 10) have a higher risk of epilepsy that lasts into adult life***(Sun et al., 2006)***.

Aim of the work

The present research aims at providing an updated review of neonatal epilepsy. All aspects of the problem will be covered in a recent comprehensive way to shed light on this critical neonatal problem. Recent diagnostic approaches and therapeutic interventions will be reviewed.

BRAIN DEVELOPMENT

EMBRYOLOGGY

At the third week, a thickening of the ectoderm appears known as the neural plate, which will form the neural groove which has two elevated edges called the neural folds.

The neural tube cranial to the fourth pair of somites develops into the brain. Fusion of the neural folds in the cranial region and closure of the rostral neuropore forms three primary brain vesicles from which the brain develops. the three primary brain vesicles form the:

- forebrain(prosencephalon)
- midbrain(mesencephalon)
- hindbrain(rhombencephalon)

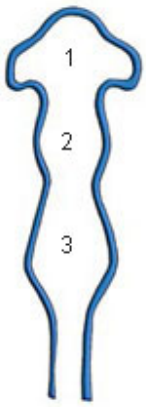

Figure1:Neural tube (cited from google images)

1.Prosencephalon

2.Mesencephalon

3.Rhombencephalon