Plasma Brain Derived Neurotrophic Factor (BDNF) Level of Full Term Newborns With Perinatal Hypoxia

Thesis submitted for partial fulfillment
of
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By

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AAP	*American academy of pediatrics*
AMP	*Adenosine monophosphate*
ADP	*Adenosine diphosphate*
α-EEG	*Amplitude-integrated Electroencephalography*
AKT	*Serine therionine protein kinase*
ATP	*Adenosine triphosphate*
BAEPs	*Brainstem auditory evoked potentials*
BDNF	*Brain derived neurotrophic factor*
BP	*Blood pressure*
BUN	*Blood urea nitrogen*
CA+٢	*Calcium*
cAMP	*Cyclic AMP*
cGMP	*Cyclic guanosine monophosphate*
CK-MB	*Creatine kinase myocardial bound*
CNS	*Central nervous system*
CNTF	*Ciliary neurotrophic factor*
CO ٢	*Carbon dioxide*
CP	*Cerebral palsy*
CPP	*Cerebral perfusion pressure*
CPR	*Cardiopulmonary resuscitation*
Cr	*Creatinine*
CSF	*Cerebrospinal fluid*
CT	*Computed tomography*
CT-١	*Cardiotrophin - ١*
cTnI	*Cardiac troponin I*
cTnT	*Cardiac troponin T*
CRE	*cAMP response element*
CREB	*cAMP response element binding protien*
DIC	*Disseminated intravascular coagulation*
DNA	*Deoxy ribonucleic acid*
DRG	*Dorsal root ganglion*
DWI	*Diffusion weighted image*
EEG	*Electroencephalograph*
ERK	*Ras/extracellular signal regulated kinase*
FE	*Fractional excretion*

GABA	*γ-aminobutyric acid*
GDNF	*Glial cell derived neurotrophic factor*
GFP	*Green fluorescent protien*
GIT	*Gastrointestinal tract*
GLU	*Glutamate*
GM	*Monosialogangliosides*
H+	*Hydrogen ion*
HIE	*Hypoxic ischemic encephalopathy*
HGF	*Hepatocyte growth factor*
ICH	*Intracranial hemorrhage*
ICP	*Intracranial pressure*
Ig	*immunoglobulin*
IL-٦	*Interleukin - ٦*
IP٣	*Inositol tri-phosphate*
IPSCs	*Inhibitory postsynaptic currents*
IVHge	*Intraventricular hemorrhage*
KA-AMPA	*Kainite-a-amino-٣-hydroxy-٥-methyl-٤-isoxazole-propionic acid*
LIF	*Leukaemia inhibitory factor*
LTD	*Long term depression*
LTP	*Long term potentiation*
MAPK	*Mitogen activated protein kinase*
MeCP٢	*Methyl CpG-binding protein ٢*
MEK	*MAPK/ERK kinase*
MOD	*Multiorgan dysfunction*
MRI	*Magnetic resonance imaging*
mRNA	*Messenger ribonucleic acid*
MRS	*Magnetic resonance spectroscopy*
MSP	*Macrophage stimulating protien*
NAA	*N-acetyl aspartate*
NE	*Neonatal encephalopathy*
NEC	*Necrotizing enterocolitis*
NGF	*Nerve growth factor*
NMDA	*N-methyl-D-aspartate receptor*
NO	*Nitric oxide*
NSE	*Neuron specific enolase*
NT٣	*Neurotrophin ٣*
O٢	*Oxygen*

OSM	*Oncostatin-M*
PCO۲	*Partial pressure of carbon dioxide*
PET	*Positron emission tomography*
PKC	*Protein kinase C*
PLC	*Phospholipase C*
PMR	*Phosphorus magnetic resonance*
P۷۵NTR	*Low affinity neurotrophin receptor*
PO۲	*Partial pressure of oxygen*
PSD۹۵	*Postsynaptic marker*
PVL	*Periventricular leukomalacia*
Raf	*MAP kinase kinase kinase*
Ras	*GTP-binding protien*
RGCs	*Retinal ganglion cells*
RI	*Resistive index*
Rsk	*Ribosomal S٦ kinase*
SD	*Standard deviation*
SHC	*Selective head cooling*
Shc	*Adaptor protein with SH۲ domain*
SIADH	*Syndrome of inappropriate antidiuretic hormone secretion*
SOS	*Son of sevenless, nucleotide exchange factor*
SPECT	*Single photon emission computed tomography*
SSEPs	*Somatosensory evoked potentials*
T۱	*Truncated TrKB*
TGF-β	*Transforming growth factor - β*
TNF	*Tumor necrosis factor*
TrK	*Tyrosin kinase*
US	*Ultrasonography*
VDCC	*Voltage dependant calcium channel*
VEPs	*Visual evoked potentials*
VGCC	*Voltage gated calcium channel*
WBC	*Whole body cooling*

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Introduction
&
Aim of work

INTRODUCTION

Hypoxic–ischemic encephalopathy (HIE) is an important cause of death and disability in full-term infants. The incidence of moderate or severe hypoxic–ischemic encephalopathy has remained essentially unchanged over the past ٢٠ years, at ١.٥ to ٢ per ١٠٠٠ live births in the United States. Approximately ١٥ to ٢٠ percent of these infants will die, and ٢٠ to ٢٥ percent of those who survive will be disabled ***(Dixon et al, ٢٠٠٢)***.

In term neonates, ٩٠% of asphyxial insults occur in the antepartum or intrapartum periods as a result of placental insufficiency, resulting in an inability to provide oxygen ($O^{٢}$) to and remove carbon dioxide ($CO^{٢}$) and hydrogen ion (H+) from the fetus. The remainders are postpartum, usually secondary to pulmonary, cardiovascular, or neurologic abnormalities (***Aurora & Snyder, ٢٠٠٤***).

Mild encephalopathy carries a good prognosis, although in moderate and severe encephalopathy the risk of death or neurologic sequelae increases greatly (***Finer et al, ١٩٨١***).

Neuroprotective interventions are increasingly in the forefront of interest and have been shown to be effective in animal models. For clinical intervention, it is important to identify infants at a high risk for brain damage soon after birth and within the therapeutic window (***Vannucci et al, ١٩٩٧***).

Neurotrophic factors play crucial roles in neuroprotection; neurotrophins promote survival and can reduce apoptosis in many populations of neurons ***(Hetman et al, ٢٠٠٠)***. Nerve growth factor, brain derived neurotrophic factor (BDNF), and neurotrophin ٣ ($NT^{٣}$) are neurotrophins that act on tyrosine kinase (Trk) A, Trk B, activities, neurotrophins play important roles in axon growth during development ***(Tucker et al, ٢٠٠١)***, higher neuronal

functions ***(Chao, ٢٠٠٠)***, morphologic differentiation, and neurotransmitter expression ***(Takei et al, ١٩٩٨)***.

Thus, neurotrophins may play important role in antenatal and postnatal brain development ***(Korhonen et al, ١٩٩٨)***.

In addition, BDNF has been demonstrated to decrease tissue loss in brain when administered after hypoxic-ischemic injury in neonatal animals ***(Cheng et al, ١٩٩٧), (Ferrer et al, ٢٠٠١)***.

Circulating BDNF levels correlate with cortical BDNF levels in newborn rats ***(Karege et al, ٢٠٠٢)***.

Thus, questions remain concerning the presence and significance of neurotrophins during the perinatal period and especially in relation to factors that may cause neurologic insults in the developing brain. Proposed initial steps to address these questions involve analyzing neurotrophin levels in umbilical cord blood in newborns with perinatal hypoxia.

Aim of the work

The aim of the present work is To assess cord blood BDNF level in full term newborns with perinatal asphyxia, to follow up its level during reperfusion phase and to study its possible relation to the development and severity of HIE .

Review Of Literature