Studying The Use Of Magnesium Sulphate For Brain Protection In Traumatic Head Injury

Thesis

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By

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Abstract

The current study describes the significance of supplemental magnesium for brain protection after traumatic brain injury .In this study, 300 adult patients with mild , moderate or severe traumatic brain injury were randomly assigned one of two doses of magnesium or placebo within 8 h of injury and continuing for 5 days. Magnesium doses were targeted to achieve serum magnesium range of 4·0 mEq/L. The outcome was a composite of mortality, seizures, time of stay in hospital and functional measures assessed up to 6 months after injury.

The conclusion was that "Parenteral magnesium sulphate by intravenous infusion within the first 8 hours after bolus dose in head trauma for the first 5 days trying to keep serum level of magnesium around 4 mEq/L appears to improve survival , reduce early and late seizures , shorten period of hospital stay in all patients with traumatic head injury , and is associated with better favorable outcome and less disability at 6 months in patients with GCS 9-12 ,without any apparent significant adverse effects".

Keywords: Traumatic brain injury, Magnesium sulphate, Outcome

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LIST OF ABBREVIATIONS

Abbreviation	The Full Term
ABCs	Airway, Breathing, Circulation.
ABGs	Arterial Blood Gases .
ADH	Anti-Diuretic Hormone.
AF	Atrial Fibrillation .
AMPA	(2-Amino-3-(5-Methyl-3-Oxo-1,2- Oxazol-4-Yl) Propanoic Acid)
AMI	Acute Myocardial Infarction .
ARDS	Adult Respiratory Disress Syndrome.
ASH	Aneurysmal Subarachnoid Hemorrhage .
ATP	Adenosine Tri-Phosphate
AV	Atrioventricular.
$AVDO_2$	Arteriovenous Difference Of Oxygen.
AVN	Atrioventricular Node.
BBB	Blood Brain Barrier

BP	Blood Pressure.
CA	Cardiopulmonary Arrest .
CBC	Complete Blood Count.
CBF	Cerebral Blood Flow.
CBV	Cerebral Blood Volume.
CDI	Central Diabetes Insipidus .
$CMRO_2$	Cerebral Matebolic Rate Of Oxygen
CNS	Central Nervous Sysem.
CO_2	Carbon Dioxide
COX-2	Cyclooxygenase-2 .
CPP	Cerebral Perfusion Pressure.
CSF	Cerebrospinal Fluid
CSW	Cerebral Salt Wasting.
CT scan	**C**omputerized **T**omography.
CVP	Central Venous Pressure.
CVR	Cerebral Vascular Resistance.
CVS	Cardiovascular System .
DCI	Delayed Cerebral Ischemia .
DIC	Disseminated Intravascular Coagulation .
DNA	Deoxyribonucleic Acid ()
ECF	Extracellular Fluid.
ECG	Electrocardiogram.

EEG	Electroencephalogram.
ELISA	Enzyme-Linked Immunosorbent Assay .
EPO	Erythropoietin .
EVD	External Ventricular Drainage
GABA	Gamma-Amino Butyric Acid.
GCS	Glasgow Coma Score.
GINA	Global Initiative For Asthma
GIT	Gastro-Intestinal Tract.
GOS	Glasgow Outcome Scale .
GOSE	Extended Glasgow Outcome Scale .
HMGCoA	3-Hydroxy-3-Methy Glutaryl Coenzyme A .
H_2O_2	Hydrogen Peroxide
HTS	Hypertonic Saline
ICF	Intracellular Fluid.
ICP	Intra Cranial Pressure.
ICU	Intensive Care Unit.
Ig	Immunoglobulin .
IL	Interleukin.
IV	Intravenous.
LMWH	Low-Molecular Weight Heparin.
LQTS	Long QT Syndrome .
MAP	Mean Arterial Blood Pressure.

Mg	Magnesium .
MgSO4	Magnesium Sulfate.
MI	Myocardial Infarction .
MMP-1	Matrix Metalloproteinase-1.
MSCs	Mesenchymal Stromal Cells.
NaCl	Sodium Chloride
NGF	Nerve Growth Factor .
NMDA	N-Methyl-D-Aspartic Acid Or N-Methyl-D-Aspartate
NO	Nitric Oxide.
NOS	Nitric Oxide Synthase.
NTF	Neurotrophic Factors .
O_2	Oxygen.
$PaCO_2$	Symbol For Partial Pressure Of Carbon Dioxide In Arterial Blood.
PaO_2	Symbol For Partial Pressure Of Oxygen In Arterial Blood.
PEEP	*Positive End Expiratory Pressure*
PPHN	Persistent Pulmonary Hypertension In Newborn .
PTH	Parathormone Hormone.
PVI	Pressure Volume Index.
RNA	Ribonucleic Acid.
ROSC	Return Of Spontaneous Circulation.
RVM	Rostral Ventrolateral Medulla
SaO_2	Peripheral Oxygen Saturation.

SD	Standard Deviation.
SIADH	Syndrome Of Inappropriate Anti-Diuretic Hormone Secretion.
sICAM	Soluble Intercellular Adhesion Molecules .
$SjVO_2$	Juglar Oxygen Saturation.
SPO_2	Saturation Of Oxygen In The Peripheral Blood.
STEMI	ST-Elevation Myocardial Infarction .
TBI	Traumatic Brain Injury.
TdP	Torsades De Pointes .
TH	Therapeutic Hypothermia .
TICU	Trauma Intensive Care Unit .
Tmax	Maximum Tubular Reabsorption Rate .
VF	Ventricular Fibrillation .
VIP	Vasoactive Intestinal Peptide
VT	Ventricular Tachycardia.
UH	Unfractionated Heparin .

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Introduction

Traumatic brain injury (TBI ,also called **intracranial injury**) occurs when an outside force injures the brain . Traumatic Brain Injury can be classified based on severity (mild, moderate ,or severe), mechanism (closed or penetrating head injury), or other features. Head injury usually refers to TBI, but is a broader category because it can involve damage to structures other than the brain, such as the scalp and skull . Traumatic brain injury is a major cause of death and disability worldwide, especially in young people. Causes include falls, vehicle accidents, and violence . Prevention measures include use of technology to protect those who are in accidents , such as seat belts and sports or motorcycle helmets, as well as efforts to reduce the number of accidents, such as safety education programs and enforcement of traffic laws. [1]

Traumatic Brain Injury (TBI), a clinical problem treated frequently by medical community, is a major cause of disability, death, and economic cost to our society. In the past two decades, we have increased remarkably our understanding of the pathophysiology of TBI [2]

One of the central concepts that emerged from clinical and laboratory research is that all neurological damage does not occur at the moment of impact, but evolves over the ensuing hours and days , Furthermore, we now recognize the deleterious effects of these various delayed insults to the injured brain at the clinical and biochemical levels [3]

This has led to an interest in developing better monitoring and treatment methods as well as the development of new pharmaceuticals, all of which show great promise in improving the outcome for patients who have suffered a brain injury

Prehospital care and emergency department treatment of patients with neurotrauma may have profound importance in their ultimate morbidity and mortality. Many key individuals provide critically important patient care in the early minutes and hours after trauma, including appropriately credentialed emergency physicians, anesthesiologists, emergency medical technicians and paramedics, and emergency department and operating room nurses, among others, whose skills and training are essential in the management of these critically injured patients [(2)]

Over the past 30 years, remarkable progress has been made in improving outcome from traumatic brain injury (TBI). Although many etiologies for such improvement have been suggested, it is unclear what changes actually affected the improvement in outcome. Despite the fervor for laboratory investigations of TBI models, it is sobering to recognize that no treatments have come from bench to bedside. As such, there are no magic bullets in the treatment of central nervous system (CNS) trauma in general, and TBI in particular. Instead, it appears to be a combination of many improvements in brain injury care, trauma systems, and critical care that has produced the decrease in mortality [(4)]

Magnesium ions are essential to all living cells. As the second most abundant intracellular cation, magnesium has a crucial role in fundamental metabolic processes such as DNA and protein synthesis, oxidative phosphorylation, enzyme function, ion channel regulation, and neuromuscular excitability. [(5)]

Magnesium is one of the four major cations in the human body and the second most abundant within the cell. Observational studies have shown the fundamental role of magnesium in treatment of different cardiovascular disorders, connected with magnesium deficiency. As co-factor of many enzymes, especially those involved in phosphate transfer, it plays a role in regulation of intracellular reactions in the organism. By influence on sodium pump and calcium pump, it regulates flowing of Na^+, Ca^{2+}, K^+ ions through channels in cell membrane and therefore, it decreases lack of K^+ ions, protects the cell from Ca^{2+} ions overloading and inhibits sodium influx into the cell. [(6)]

Magnesium is an important cofactor for many biological processes, such as protein synthesis, nucleic acid stability, or neuromuscular excitability. [(7)]

Magnesium role is achieved through two important properties of magnesium; the ability to form chelates with important intracellular anionic-ligands, especially ATP, and its ability to compete with calcium for binding sites on proteins and membranes. [(8)]

Magnesium is an often overlooked electrolyte that is essential to life. Magnesium plays a role in more than 300 enzymatic reactions and is critically involved in energy metabolism, glucose utilization, protein synthesis, fatty acid synthesis and breakdown, ATPase functions, and virtually all hormonal reactions. Magnesium is closely involved in maintaining cellular ionic balance through its association with sodium, potassium, and calcium. [(9)]

Aim of work :

Study the effect of magnesium sulfate on the patients of traumatic brain injury admitted to ICU within 8 hours after injury , giving Magnesium sulfate daily for 5 days reaching magnesium blood level of approximately 4 mEq /L

The outcome is studied in terms of mortality ,Seizures , time of stay in hospital and ICU and functional disability.