MAGNESIUM IN INTENSIVE CARE UNIT HYPOMAGNESEMIA , HYPERMAGNESEMIA & THERAPEUTIC USES

Essay

Submitted for partial fulfillment of the master degree of the
Intensive Care Medicine

By:

AbdulRahman Nasser Ali
(M. B., B.Ch)

Supervised by

Prof. Dr. Bahira Mohammed Tawfeek
Professor of Anaethesiology & Intensive Care Medicine
Faculty of Medicine, Ain Shams University

Dr. Walid Ahmed Mansour
Lecturer of Anaethesiology & Intensive Care Medicine
Faculty of Medicine, Ain shams University

Dr. Mohamed Sayed Shorbagy
Lecturer of Anaethesiology & Intensive Care Medicine
Faculty of Medicine, Ain shams University

Faculty of Medicine
Ain Shams University
٢٠١٥

قالُوا سُبْحَانَكَ لاَ عِلْمَ لَنَا إِلاَّ مَا عَلَّمْتَنَا إِنَّكَ أَنتَ الْعَلِيمُ الْحَكِيمُ

صدق الله العظيم

سورة البقرة آية (٣٢)

Acknowledgement

First of all, all gratitude is due to **God** *almighty for blessing this work, until it has reached its end, as a part of his generous help, throughout my life.*

Really I can hardly find the words to express my gratitude to **Prof. Dr. Bahira Mohammed Tawfeek AbdelRahman** *Professor of Anesthesiology and Intensive Care Medicine, Faculty of Medicine, Ain Shams University, for her supervision, continuous help, encouragement throughout this work and tremendous effort she has done in the meticulous revision of the whole work. It is a great honor to work under her guidance and supervision.*

I would like also to express my sincere appreciation and gratitude to **Dr. Walid Ahmed Mansour** *Lecturer of Anesthesiology and Intensive Care Medicine, Faculty of medicine, Ain Shams University, for his continuous directions and support throughout the whole work.*

I would also like to express my deep appreciation to **Dr. Mohammed Sayed Shorbagy** *Lecturer of Anaethesiology & Intensive Care Medicine, Faculty of Medicine-Ain Shams University, for his great kindness, constant assistance and guidance.*

Last but not least, I dedicate this work to my family, whom without their sincere emotional support, pushing me forward this work would not have ever been completed.

AbdulRahman Nasser Ali

Contents

List of Abbreviations

ABCs	:	Airway , Breathing and Circulation
ABG	:	Arterial blood gases
ACS	:	Antenatal corticosteroids
ADHH	:	Autosomal-dominant hypocalcemia with hypercalciuria
APD	:	Action potential duration
APs	:	Action potentials
ATP	:	Adenosine triphosphate
ATPase	:	Adenosine Triphosphatase enzyme
AV	:	Atrioventricular
C-AMP	:	Cyclic Adenosine Monophosphate
CASR	:	Gene encodes for calcium-sensing receptor
CaSR	:	Calcium-sensing receptor
CBC	:	Complete blood count
cc	:	cubic centimeter
CCr	:	creatinine clearance
CKD	:	Chronic kidney disease
CLC-Kb	:	Kidney specific choloride channel
CLCNKB	:	Chloride channel voltage-sensitive kb
CLDN١٦	:	Claudin ١٦ gene
DCT	:	Distal convoluted tubule
DNA	:	Deoxyribonucleic acid
DTRs	:	Deep tendon reflexes
EADs	:	Early after depolarization activities
ECG	:	Electrocardiography
ED	:	Emergency department
EGF	:	Epidermal growth factor
EGFR	:	Epidermal growth factor receptor
EP	:	Electrophysiological
ERP	:	Effective refractory period

List of Abbreviations (Cont.)

ESRD	:	End-stage renal disease
Fab	:	Digoxin antidote
FDA	:	US Federal Drug Administration FE : Fractional excretion
FEMg	:	Fractional excretion of magnesium
FGF-23	:	Fibroblast growth factor-23
FHHNC	:	Familial hypomagnesemia with hypercalciuria and nephrocalcinosis
FXYD٢	:	A gene encoding Sodium/potassium-transporting ATPase gamma chain
GFR	:	Glomerular filtration rate
HD	:	Hemodialysis
HSH	:	Hypomagnesemia with secondary hypocalcemia
ICU	:	Intensive care unit
IDH	:	Isolated dominant hypomagnesemia
iPTH	:	Intact Parathyroid hormone
IRH	:	Isolated recessive hypomagnesemia
ISIS-٤	:	Fourth International Study of Infarct Survival
IV	:	Intravenous
LIMIT-٢	:	Second Leicester Intravenous Magnesium Intervention Trial
MDI	:	Metered-dose inhaler
MFM	:	Maternal-fetal medicine
MgSO٤	:	Magnesium sulphate
NCC	:	Na^+–Cl^- cotransporter
NICU	:	Neonatal intensive care unit
NKCC	:	Na^+ K^+ Cl^- cotransporter
PCT	:	Proximal convoluted tubule
PD	:	Pritoneal dialysis
PE/E	:	Pre-eclampsia/Eclampsia

List of Abbreviations (Cont.)

PPIs	:	Proton-pump inhibitors
PTH	:	Parathyroid hormone
RNA	:	Ribonucleic acid
ROMK	:	Renal outer medullary K^+ channel
SA	:	Sinoatrial node
SLC١٢A٣	:	Gene encodes the thiazide-sensitive NaCl cotransporter
SNRT	:	Sinus node recovery time
TAL	:	Thick ascending limb of the loop of Henle
TRP	:	Transient receptor potential
TRPM	:	Transient receptor potential cation channel

List of tables

List of Figures

Introduction

Magnesium is the second-most abundant intracellular cation and, overall, the fourth-most abundant cation. It plays a fundamental role in many functions of the cell, including energy transfer, storage, and use; protein, carbohydrate, and fat metabolism; maintenance of normal cell membrane function; and the regulation of parathyroid hormone (PTH) secretion. Systemically, magnesium lowers blood pressure and alters peripheral vascular resistance. ***(Drueke et al , ٢٠٠٧).***

Almost all enzymatic processes using phosphorus as an energy source require magnesium for activation. Magnesium is involved in nearly every aspect of biochemical metabolism (eg, deoxyribonucleic acid [DNA] and protein synthesis, glycolysis, oxidative phosphorylation). Almost all enzymes involved in phosphorus reactions (eg, adenosine triphosphatase [ATPase]) require magnesium for activation. Magnesium serves as a molecular stabilizer of ribonucleic acid (RNA), DNA, and ribosomes. Because magnesium is bound to adenosine triphosphate (ATP) inside the cell, shifts in intracellular magnesium concentration may help to regulate cellular bioenergetics, such as mitochondrial respiration. ***(Drueke et al , ٢٠٠٧).***

Extracellularly, magnesium ions block neurosynaptic transmission by interfering with the release of acetylcholine. Magnesium ions also may interfere with the release of catecholamines from the adrenal medulla. Magnesium has been proposed as an endogenous endocrine modulator of the catecholamine component of the physiologic stress response. ***(Drueke et al , ٢٠٠٧).***

Magnesium deficiency has been reported in ٢٠ to ٦٥% of patients in the ICU. Reduction in serum total magnesium on

admission to the ICU has been shown to be associated with increased morbidity and mortality. ***(Esen& Telci, ٢٠٠٨).***

Abnormalities of magnesium levels, such as hypomagnesemia, can result in disturbances in nearly every organ system and can cause potentially fatal complications (eg, ventricular arrhythmia, coronary artery vasospasm, sudden death). Despite the well-recognized importance of magnesium, low and high levels have been documented in ill patients,[٢] as a result of which, magnesium has occasionally been called the "forgotten cation". ***(Martin et al, ٢٠٠٩).***

Studies have shown the effectiveness of magnesium in eclampsia and preeclampsia, arrhythmia, severe asthma, and migraine. Other areas that have shown promising results include lowering the risk of metabolic syndrome, improving glucose and insulin metabolism, relieving symptoms of dysmenorrhea, and alleviating leg cramps in women who are pregnant. The use of magnesium for constipation and dyspepsia are accepted as standard care despite limited evidence. ***(Mary et al, ٢٠٠٩).***

Aim of the Work

This work will discuss current concept about the Magnesium electrolyte highlighting its serum level disturbances effect and its therapeutic uses in critically ill patients.

Chapter I

Hypomagnesemia in ICU

The total body magnesium content of an average adult is ٢٥ g, or ١٠٠٠ mmol. Approximately ٦٠% of the body's magnesium is present in bone, ٢٠% is in muscle, and another ٢٠% is in soft tissue and the liver. Approximately ٩٩% of total body magnesium is intracellular or bone-deposited, with only ١% present in the extracellular space. Seventy percent of plasma magnesium is ionized or complexed to filterable ions (eg, oxalate, phosphate, citrate) and is available for glomerular filtration, while ٢٠% is protein-bound. Normal plasma magnesium concentration is ١.٧-٢.١ mg/dL (٠.٧-٠.٩ mmol, or ١.٤-١.٨ mEq/L).***(Drueke et al, ٢٠٠٧)***.

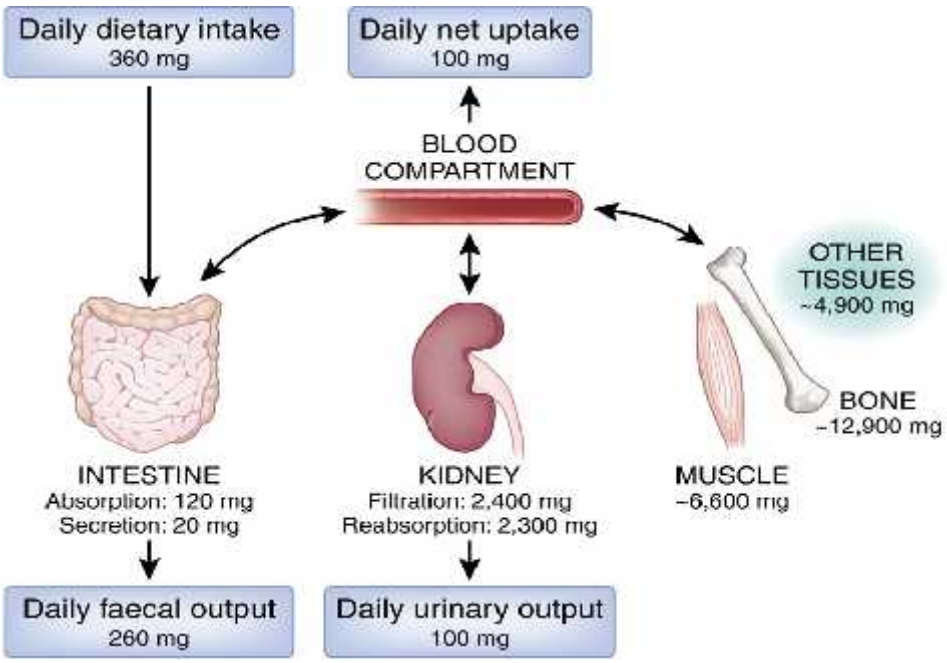

Fig. (١): Magnesium homeostasis.***(Jahnen-Dechent & Ketteler, ٢٠١٢)***.