PHOSPHORUS DISORDERS IN CRITICALLY ILL PATIENTS

Essay
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LIST OF ABBREVIATIONS

Abb.	Full term
ADHR	Autosomal dominant hypophosphatemic rickets
AHO	Albright hereditary osteodystrophy
AKA	Alcoholic ketoacidosis
ALL	Acute lymphocytic leukemia
AML	Acute myeloid leukemia
ARF	Acute respiratory failure
ARHR	Autosomal recessive hypophosphatemic rickets
ASARM	Acidic serine-aspartate-rich MEPE
ATP	Adenosine triphosphate
BBM	Brush border membrane
BUN	Blood urea nitrogen
cAMP	Cyclic adenosine monophosphate
CaSR	Calcium transmembrane domain receptor
(Ca)10(PO4)(OH)2	Crystallin hydroxyapatite
CCT	Cortical collecting tubule
CKD	Chronic kidney disease
CNS	Central nervous system
COPD	Chronic obstructive pulmonary disease
CYP450	Cytochrome P450
DKA	Diabetic ketoacidosis
EBCT	Electron beam computed tomography
ECF	Extracellular fluid
ECM	Extracellular matrix
ED	Emergency department
ESRD	End stage renal disease
FDA	Food and diet administration
FGF-23	Fibroblast growth factor-23

LIST OF ABBREVIATIONS (Cont…)

Abb.	Full term
FGF-7	Fibroblast growth factor-7
FS	Fanconi syndrome
GBS	*Guillain Barré syndrome*
GFR	Glomerular filteration rate
GHRH	Growth hormone releasing hormone
GI	Gastro-intestinal
GM-CSF	Granulocyte-macrophage colony-stimulating factor
H2PO4	Dihydrogen phosphate
HHRH	Hereditary hypophosphatemic rickets with hypercalcuria
HPO4	Hydrogen phosphate
ICU	Intensive care unit
IDBP	Intermediate vitamine D binding protein
IFN gamma	Interferon gamma
IGF-1	Insulin growth factor-1
IMCD	Inner medullary collecting duct or tubule
LDL-C	Low density lipoprotein-c
MDCT	Multidetector computed tomography
MEPE	Matrix Extracellular Phosphoglycoprotein
NAD	Nicotinamide adenine dinucleotide
NPT 1,2,3	Sodium phosphate co-transporter 1,2,3
NPT2a	Sodium phosphate co-transporter- a
NPT2b	Sodium phosphate co-transporter-b
NPT2c	Sodium phosphate co-transporter-c
ODC	Oxygen dissociation curve
OK-Cells	Opossum kidney cells
P50	Oxygen tension at 50% oxygen saturation
PCT	Proximal convoluted tubule

LIST OF ABBREVIATIONS (Cont…)

Abb.	Full term
PHEX	Phosphate regulating gene with homologies to endopeptidases on the X chromosome
PHP	Pseudohypoparathyroidism
Pi	Inorganic phosphate
Pit-1	Phosphate transporter-1
PO4	Phosphate ion
PST	Proximal straight tubule
PTH	Parathyroid hormone
RFS	Refeeding syndrome
RGD	Integrin-binding tripeptide Arg-Gly-Asp (RGD) motif
sFRP	Soluble Frizzled-related Protein
SIADH	Syndrome of inappropriate antidiuretic hormone
SLC-34	Soluble carrier 34 family
STC-1	Stanniocalcin-1
TIO	Tumor induced osteomalacia
TLS	Tumor lysis syndrome
TmP/GFR	Maximal tubular reabsorption of phosphate
TNSALP	Tissue-nonspecific isoenzyme of alkaline phosphatase
TPN	Total parenteral nutrition
TSH	Thyroid stimulating hormone
U-Pi	Urinary phosphate
Uv-B	Ultra-violet rays beta
VDBP	Vitamine D binding protein
XLH	X-linked hypophosphatemic richets
1,25-(OH)2D3	1,25-dihydroxy cholecaciferol
1,3-DPG	1,3 diphosphoglycerate
2,3-DPG	2,3 diphosphoglycerate
7-DHC	7- dehydrocholesterol

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INTRODUCTION

Phosphorus plays an important role in growth, development, bone formation, acid - base regulation, and cellular metabolism ***(Yanagawa et al., 1994)***.

In a healthy 70 kg adult, the total body phosphorus content is around 700 gm of which about 80% is present in the skeleton as crystalline hydroxyapatite, 9 %in the skeletal muscle, 10.9 % in the viscera, and 0.1% in the extracellular fluid ***(Gaasbeek and Meinders, 2005).***

The kidney adjusts urinary excretion of phosphate according to phosphate intake and maintains the serum phosphate concentration within a narrow range ***(Prie' and Friedlander, 2010).***

Hormonal control is provided mainly by parathyroid hormone, calcitonine and 1,25 dihydroxycholecalciferol ***(Bugg and Jones, 1997)***.

Electrolyte disorders frequently develop in critically ill patient during course of stay in intensive care unit. Phosphate disorders are commonly encountered electrolyte disorders, for which many causative factors are present in critically ill patient ***(Geerse et al., 2010).***

Hypophosphatemia is defined as serum phosphorus level below 2.5 mg/dl in adult and below 4mg/dl in children ***(Miller and Slovis, 2000)***.

It is caused by decrease intestinal absorption, increase renal excretion, or internal redistribution. It is associated with respiratory muscle dysfunction, resulting in acute respiratory failure and weaning problems, and also can lead to myocardial dysfunction and arrhythmias, other effects include hematologic dysfunction, insulin resistance, number of neuromuscular symptoms, rhabdomyolysis and central pontine myelinolysis ***(Geerse et al., 2010).***

Serum phosphorus level > 4.5 mg/dl defines hyperphospha-temia. The most common cause of it is decrease phosphate excretion due to renal insufficiency. In addition to reduce phosphate excretion, higher dietary intake of phosphate will also contribute, severe hypocalcemia, tetany and ectopic calcification are the most serious result of hyperphosphatemia ***(Blokker, 2008).***

AIM OF THE WORK

To identify the incidence, symptoms, effects and treatment of phosphorus disorders in critically ill patients and whether a certain treatment strategy is superior.

PHOSPHORUS

Phosphorus is the chemical element that has the symbol P and atomic number 15. A multivalent non-metal of the nitrogen group, phosphorus as a mineral is almost always present in its maximally oxidized state, as inorganic phosphate rocks. Elemental phosphorus exists in two major forms, white phosphorus and red phosphorus but due to its high reactivity, phosphorus is never found as a free element on earth ***(Piro et al., 2006).***

Phosphorus plays a critical role in cellular biology**.** Many cellular processes require phosphorus in one form or another and include nucleic acid synthesis and metabolism, energy metabolism, cellular signaling**,** membrane integrity**,** muscle function, enzyme activity, lipid metabolism, and bone mineralization ***(Berndt and Kumar, 2009).***

Dietary sources

Phosphorus **(P_i)** is abundant in many food sources, as foods can contain both natural phosphate and phosphate additives. Foods high in protein are also high in natural phosphate ***(Paturi et al., 2008).***

Approximately 1000 mg of phosphorus is the recommended daily allowance for healthy adults, with an average of 800 mg for normal children. Dietary sources of phosphorus include protein-rich foods, cereals, and nuts ***(Crook et al., 2001).***

Normal healthy individuals can tolerate P_i intakes of up to 3 gm/d. Although P_i is widely available virtually in all foods, P_i intake from dairy, grain and meat products covers 75% of the total average daily intake of P_i in ***(Paturi et al., 2008).***

Phosphorus homeostasis:

The main P_i homeostasis regulation sites are the gastrointestinal tract (absorption organ), kidneys (excretion organ) and bone (storage organ). The most important regulation occurs in the kidneys, and homeostasis is achieved by excreting P_i in urine. The quantitative aspects of phosphorus homeostasis in humans are shown in **(Figure 1.1&1.2)** ***(Berndt and Kumar, 2007).***

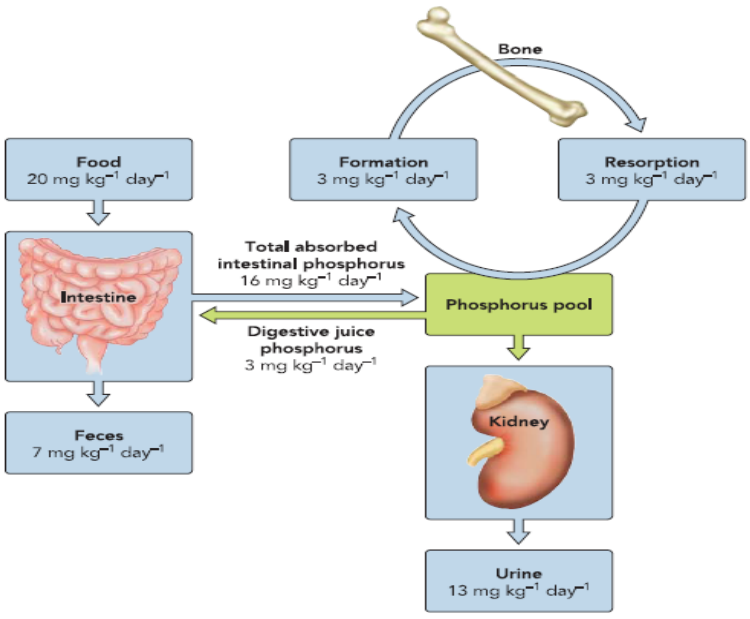

Figure (1.1): Phosphorus homeostasis in normal humans ***(Berndt and Kumar, 2007).***

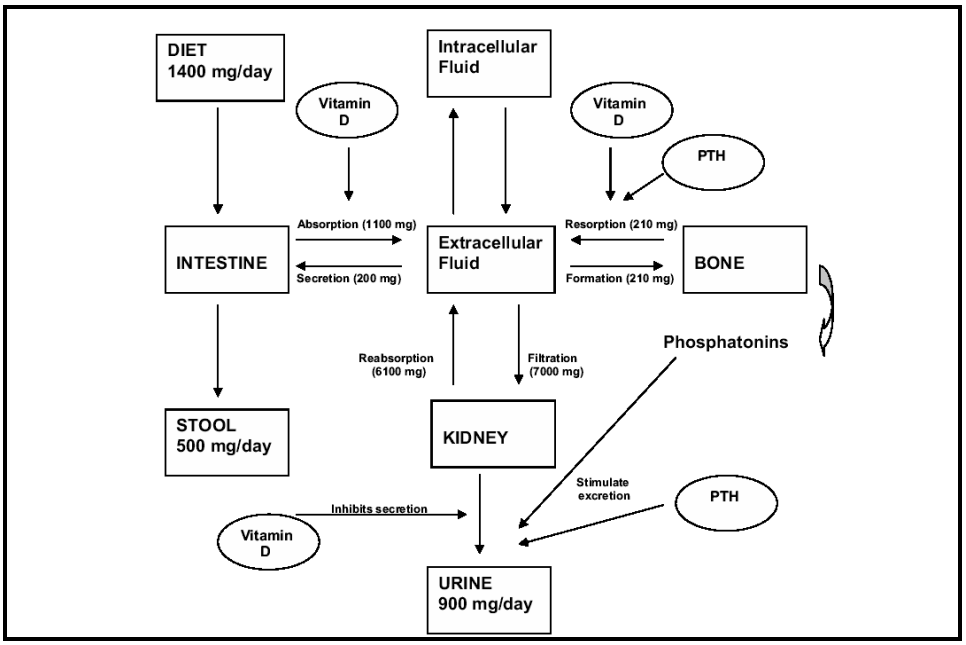

Figure (1.2): Summary of the phosphate metabolism for a normal adult in neutral phosphate balance. The relevance of the phosphatonins in the normal homeostasis and under pathologic conditions has to be established. Bone is one of the sources of the phosphatatonins. PTH= parathyroid hormone ***(Gaasbeek and Meinders, 2005).***

a) Phosphorus metabolism:

Phosphorus absorption:

Approximately 70% of dietary phosphorus is absorbed, principally in the jejunum. This occurs through one of two ways; a passive intercellular route and a facilitated transport intracellular route. Phosphorus absorption is described as being minimally regulated. At issue is whether most of the absorption is passive or facilitated ***(Takeda, 2004).***

Paracellular/intercellular transport is favored electrochemically because the phosphorus concentration of