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REVIEW

Hyperphosphatemia Management in Patients with Chronic Kidney Disease

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Abstract Hyperphosphatemia in chronic kidney disease (CKD) patients is a potentially life altering condition that can lead to cardiovascular calcification, metabolic bone disease (renal osteodystrophy) and the development of secondary hyperparathyroidism (SHPT). It is also associated with increased prevalence of cardiovascular diseases and mortality rates. To effectively manage hyperphosphatemia in CKD patients it is important to not only consider pharmacological and nonpharmacological treatment options but also to understand the underlying physiologic pathways involved in phosphorus homoeostasis. This review will therefore provide both a background into phosphorus homoeostasis and the management of hyperphosphatemia in CKD patients. In addition, it will cover some of the most important reasons for failure to control hyperphosphatemia with emphasis on the effect of the gastric pH on phosphate binders efficiency.

Contents

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1. Introduction

Hyperphosphatemia in chronic kidney disease (CKD) patients is a potentially life altering condition that can lead to cardiovascular calcification, metabolic bone disease (renal osteodystrophy) and the development of secondary hyperparathyroidism (SHPT). To effectively manage hyperphosphatemia in CKD patients it is important to not only consider pharmacological and non-pharmacological treatment options but also to understand the underlying physiologic pathways involved in phosphorus homoeostasis. This review will therefore provide both a background into phosphorus homoeostasis and the management of hyperphosphatemia in CKD patients. In addition, it will cover some of the most important reasons for failure to control hyperphosphatemia with emphasis on the effect of the gastric pH on phosphate binders efficiency.

Phosphorus is the second most abundant element in the human body after calcium (Bellasi et al., 2006). The majority (85%) of phosphorus is found in bone and teeth as hydroxyapatite (Uribarri, 2007; Bellasi et al., 2006), 14% is located intracellularly as organic phosphate compounds; with the remaining 1% of the total body phosphate located extracellularly, mainly as inorganic phosphate (Bellasi et al., 2006; Uribarri, 2007). Of the 1% located in the vascular space, 20% is protein bound (Uribarri, 2007).

Inorganic phosphate is a component of many organic compounds and cell structures such as phospholipid cell membranes, nucleic acids, and phosphoproteins (Berndt et al., 2005). It plays significant roles in many biological processes such as cell signalling, synthesis of nucleic acid, energy metabolism, membrane functions, bone mineralisation and carbohydrate metabolism (Berndt and Kumar, 2007; Xie et al., 2000). In addition, it is essential for the normal generation of red blood cells, white blood cells and platelet function (Berndt et al., 2005). Phosphate is sourced for adenosine triphosphate synthesis, a critical energy source for physiological processes such as muscle contractility, neurological activities, electrolyte transportation, and other biological reactions (Nishi et al., 2011). Given the importance of phosphate for varied and multiple biological processes, it is not surprising that phosphate homoeostasis is a complex and highly regulated processes.

2. Phosphate homoeostasis in humans

In healthy adults, most laboratories quote a normal phosphate reference concentration range of 0.80–1.45 mmol/L (Berndt and Kumar, 2007). Overall intake and excretion is determined by the net balance of ingested and absorbed phosphate from food, and phosphate excretion through the bowels and the urinary tract (Hahn et al., 1937). In addition, the plasma phosphate concentration is also influenced by the rate of bone formation and resorption, since phosphate moves in and out of the bone (Berndt et al., 2005; Weidmann, 1956; Hahn et al., 1937).

2.1. Intestinal absorption

The average ingested phosphate content from dietary intake is in the order of 20 mg/kg/day (see Fig. 1) and it is typically found in foods that are rich in protein such as dairy products, meats, eggs, and cereals as well as food additives that contain phosphate (Schaefer, 1994; Berndt et al., 2005; Bellasi et al., 2006). The bioavailability of phosphate from a vegetarian diet is relatively low compared to meat dietary protein (Moe et al., 2011). Phosphorus from plant sources is mostly in the form of phytate, which is not hydrolysable by humans due the lack of phytase enzyme and hence, is not absorbable (Moe et al., 2011). Vegetarians would therefore be expected to ingest less phosphate compared to non-vegetarians.

Of the total amount of daily ingested phosphate, 16 mg/kg/day is usually absorbed by the intestine and approximately 3 mg/kg/day is secreted back into the intestine through pancreatic and intestinal secretions (Berndt et al., 2005). The remaining 7 mg/kg/day of unabsorbed phosphate is excreted via the faecal route (Berndt et al., 2005).

The major sites for phosphate absorption are in the jejunum and ileum (Bellasi et al., 2006; Xie et al., 2000; Katai et al., 1999). The absorption process is carried out both by