Clinical Kidney Journal

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LEADING EUROPEAN NEPHROLOGY

Clinical Kidney Journal, 2021, vol. 14, no. 2, 474–475

doi: 10.1093/ckj/sfaa246
Advance Access Publication Date: 16 December 2020
Editorial Comment

EDITORIAL COMMENT

Do we need new phosphate binders in dialysis?

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ABSTRACT

Patients affected by chronic kidney disease (CKD) have a greater risk of mortality than the general population. Fatal cardiovascular events are the most frequent cause of death in CKD patients, especially in the late stages of disease. Derangement of mineral metabolism and hyperphosphataemia are currently accepted as pivotal triggers of these vascular complications. Phosphate binders represent the common strategy to counteract hyperphosphataemia in dialysis patients. Several studies have reported a reduction in mortality risk in dialysis patients receiving phosphate binders compared with untreated patients, independent of the class of binder prescribed.

Keywords: CKD-MBD, dialysis, hyperphosphataemia, phosphate binder

During the last decades, a direct and independent association between serum phosphate levels and mortality has been reported. Growing data support the fact that phosphate overload may hamper survival, directly inducing vascular and skeletal ageing. Hyperphosphataemia is accepted as a late consequence of advanced chronic kidney disease (CKD), starting with a glomerular filtration rate <30 mL/min [1]. High circulating phosphate levels have been repeatedly linked to reduced survival in observational studies conducted among dialysis cohorts [2].

Interestingly, observational data have shown that dialysis patients receiving phosphate binders were exposed to lower mortality risk compared with controls [3, 4]. Experimental and epidemiological research has shed light in the same direction, suggesting how increased phosphate concentrations may be primarily responsible for poor clinical outcomes by triggering and sustaining the CKD and mineral and bone disorder (CKD-MBD) syndrome, characterized by vascular ageing and altered mineral metabolism [5].

Phosphate binders represent the common strategy to counteract nutritional phosphate load. Unfortunately, head-to-head comparisons between phosphate binders and placebo on hard endpoints have never been conducted in dedicated randomized controlled trials. Observational data reported an almost 30% reduction of mortality risk in dialysis patients receiving phosphate binders compared with untreated patients, independent of the class of binder prescribed [4].

In the mid 80s, calcium-containing phosphate binders started to make their appearance [6]. Two compounds have been extensively used since then, calcium carbonate and calcium acetate. Calcium-containing binders (CCBs) are well tolerated, reasonably effective and have a low cost. In contrast, high doses of CCBs have been associated with increased cardiovascular calcification [7]. Lower doses might not be that harmful, but they are less effective. Their use in the presence of signs of vascular calcification should be considered very carefully and probably avoided. For this reason, non-calcium- and non-aluminum-based phosphate binders emerged [8]. Sevelamer hydrochloride initially and later carbonate have been proven to be an effective phosphate binders, showing also additional favourable effects, such as lowering low-density lipoprotein cholesterol levels, without aggravating vascular calcification

Received: 16.10.2020; Editorial decision: 19.10.2020

Comparison of available phosphate binders

	Effective	Pill burden	Pleiotropic effects	Accumulation
Aluminium	Yes	Low	None	Yes
Calcium-Ac/Carb	Yes	High	None	Yes
Sevelamer	Yes	High	Yes	No
Lanthanum	Yes	Low	None	Some
Fe-oxyhydroxide	Yes	Low	None	No

FIGURE 1: Comparison of available phosphate binders.

[9]. Unfortunately, sevelamer suffers from a high pill burden in order to achieve the desirable serum phosphorus levels, together with some gastrointestinal discomfort. Additionally, cost is another factor that might have limited its prescription in some countries.

Lanthanum carbonate is a second non-calcium-containing phosphate binder. It is a potent binder, usually needing fewer pills to achieve the desired effect. Similar to sevelamer, the cost of lanthanum is also a problem. Furthermore, lanthanum carbonate pills are chewable, a fact that, due to its taste, constitutes a major drawback for some patients since, like all phosphate binders, they should be consumed during meals [10].

More recently in Europe, the iron-based phosphate binder sucroferric oxyhydroxide (SO) has been made available to treat hyperphosphataemia in dialysis patients [11]. It is safe and effective, with minimal gastrointestinal side effects. Navarro-Gonzales *et al.* [12] investigated the efficacy and safety of SO in real clinical practice in a retrospective multicentre study that included 220 dialysis patients. Interestingly, SO as monotherapy increased to 74%, with a reduction in the average number of pills from six to two daily. Serum phosphate levels decreased from 5.8 ± 1.3 to 4.6 ± 1.2 mg/dL ($P < 0.001$), with significant control of secondary hyperparathyroidism. In addition, adverse effects, mostly gastrointestinal, were reported by only 14% of patients.

In Figure 1 we graphically represent the major characteristics of phosphate binders used in dialysis. In summary, phosphate binders should be tailored to the patient. The impact of phosphate load on survival remains a hot topic in contemporary medicine. Improving knowledge about phosphate balance and its potential toxicity is challenging, but is needed to improve the care of the general population and renal patients. Further insights are urgently needed to bridge the gaps in our knowledge of pathophysiology and epidemiology. While we wait for dedicated randomized controlled trials on the topic, current evidence is mainly observational and insufficient to recommend different interventions from those purposed in the current guidelines.

CONFLICT OF INTEREST STATEMENT

None declared.

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