Treatment of Phosphorus Balance Disorders

Walter Grünberg, Dr med vet, MS, PhD

KEYWORDS

• Hypophosphatemia • Phosphorus • Homeostasis • Cattle • Treatment

KEY POINTS

- With phosphorus (P) a predominantly intracellular electrolyte, accurately assessing the P status of an individual animal remains a challenge.
- The P concentration in serum or plasma, although widely used to diagnose P balance disorders, is an unreliable parameter for this purpose.
- In many instances, the causative relation between acute hypophosphatemia and the clinical signs associated with it are not well established.
- Organic P compounds contained in pharmaceutical products intended for parenteral treatment in food-producing animals often provide P in a form that is not effectively converted into phosphate (PO_4). These compounds are, therefore, unsuitable for P supplementation.
- Intravenous (IV) bolus infusion of sodium PO_4 salt solutions has an immediate but very short-lived effect on the serum P concentration.
- Oral supplementation of PO_4 salts presents a practical and effective treatment alternative in P-depleted animals but seems to require some degree of rumen motility.

FUNCTIONS OF PHOSPHORUS IN THE ORGANISM

P is an essential macromineral with a plethora of important biologic functions. P plays a structural role at tissue, cellular, and molecular levels of any living organism. P in bone and teeth provides these tissues with their characteristic rigidity and stability. Cellular integrity depends on P that forms an integral part of the phospholipids that form cell membranes. P is also incorporated in nucleic acid molecules, such as DNA and RNA. The regulation of metabolism on a cellular level is highly dependent on the availability of P for phosphorylation, a chemical reaction where P is added to an enzyme or other molecule, thereby modulating the biologic activity of this molecule. Energy is transported and stored within cells in the form of high-energy PO_4 bonds,

Conflict of interest disclosure: The author has no conflicts of interest to report.

Clinic for Cattle, University of Veterinary Medicine Hannover, Foundation, Bischofsholer Damm 15, 30173 Hanover, Germany
E-mail address: waltergruenberg@yahoo.com

Vet Clin Food Anim ■ (2014) ■–■
http://dx.doi.org/10.1016/j.cvfa.2014.03.002 vetfood.theclinics.com
0749-0720/14/$ – see front matter

such as ATP or creatine PO_4. PO_4 is an effective buffer in biologic fluids, such as cytosol, urine, or rumen fluid, thereby contributing to maintaining the acid-base equilibrium in the organism. By being the quantitatively most important intracellular anion, P is a major contributor to the transmembrane potential and the osmotic equilibrium between intra- and extracellular space.[1–3] In ruminants, P is an essential nutrient for ruminal microorganisms where it is required for the fermentation of cellulose and the synthesis of microbial protein.[4–6]

Phosphorus, Inorganic Phosphorus, and Phosphate

Elemental P is highly reactive and too unstable to occur as such in nature. The most commonly encountered form of P is PO_4, that is, the maximally oxidized form of P. In the body, P is present as PO_4 that is either unbound and, therefore, also called inorganic P or orthophosphate (Pi), or chemically bonded to a carbon-containing molecule, in which case it is referred to it as either organic P or organic PO_4 (Po). It is, therefore, tempting to use the terms, *P* and *PO_4*, interchangeably but, strictly speaking, Pi is the P contained in inorganic PO_4, whereas inorganic PO_4 refers to the entire unbound PO_4 molecule. Differentiating between P and PO_4 is important when concentrations of Pi are expressed on a weight rather than a molar basis (ie, in mg/dL instead of mmol/L). Whereas 1 mol of P is equivalent to 1 mol of PO_4, the masses of the atom P and the molecule PO_4 are different. The widely accepted reference range of the serum Pi concentration [Pi] is 1.4 to 2.6 mmol/L, which is equivalent to 4.0 to 8.0 mg/dL of Pi but 12.3 to 24.7 mg/dL of inorganic PO_4.[3] The reference range of 4.0 to 8.0 mg/dL thus refers to the concentration of [P] and not of PO_4.

Inorganic PO_4 in the body is present either in its divalent (HPO_4^{2-}) or its monovalent form ($H_2PO_4^-$), with the ratio HPO_4^{2-}:$H_2PO_4^-$ depending on the ambient pH. At a pH of 7.4, this ratio is approximately 4:1 but decreases with decreasing pH. The divalent form can be considered an effective buffer that is able to bind 1 H^+, whereas the monovalent form can be considered a used buffer that does not bind any more protons at the pH range normally encountered in the body.

The ammonium molybdate method is the standard clinical chemistry procedure used to determine [P] in body fluids, such as serum, plasma, whole blood, urine, or saliva, and is based on a reaction of molybdate with the PO_4 molecule to form a phosphomolybdate complex. This method specifically measures the [Pi] rather than the [P]. In contrast, P in tissue, feed, feces, or milk is generally measured using methods determining the total P content.

For phosphorylation and the synthesis of any P-containing organic molecule, the organism requires the availability of inorganic PO_4, which is the only known substrate that can be used for phosphorylation. To effectively supplement an animal with P, therefore, requires providing either inorganic PO_4 or a P-containing compound that can be readily hydrolyzed in the organism to release the inorganic PO_4.

In this article, P refers to P contained in either organic or inorganic PO_4, whereas Pi refers to P contained in inorganic PO_4 alone.

Distribution of Phosphorus in the Body

In vertebrates, 80% to 85% of the body's P is located in the skeleton, primarily in the form of insoluble salts, namely calcium phosphate ($Ca_3[PO_4]_2$) and dihydroxyapatite ($Ca_{10}[PO_4]_6[OH]_2$), which present the biologically inert storage form of P. Between 15% and 20% of the body P is distributed in fluids and soft tissues of the body, thus forming the body P pool.

The bulk of the body P pool is located in the intracellular space, whereas less than 1% of the total body P content is found in the extracellular space. The intracellular [P]