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Review Article

Phosphorus Dynamics in Ruminants - An Overview

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Abstract

By an large the objective of the present review is to provide an understanding on the complex and dynamic mechanism involved in maintenance of P homeostasis in ruminants and the complications emerge in animals due to dietary P imbalances. Phosphorus (P) is the second most required macro-mineral in an animal's diet with diverse functions in the body as compared to any other mineral. In animal diet, P is present in an inorganic and organic form. A high fraction of P is present in the form of phytate in feedstuffs of plant origin. Ruminants have substantial microbial activity in the rumen catalyzed by enzymatic phytase to break down phytate and release P in a form that can be easily absorbed along the gastrointestinal tract. Endogenously excreted salivary P in the rumen is utilized by the rumen microbes and reabsorbed again along the gastrointestinal tract. Faecal endogenous P is the main pathway of P excretion in adult ruminants in contrast to small ruminants and non-ruminants where urine is the main route of Pi excretion. Saliva is the major source of P and is correlated with certain factors like type of diet and DM intake. Rumen microbial P is the another source of faecal endogenous P that escaped solubilisation during post ruminal digestion In adult ruminants, P balance is mainly determined through regulation of apparent P digestion, P secretion in milk and regulation of P exchange between bones and blood. A variety of endocrine factors are involved in the regulation of P metabolism, and all are interrelated with feedback loops. Phosphorus and Ca metabolism in ruminants is mainly regulated by parathyroid hormone, vitamin D_3 and calcitonin. Phosphorus must be balanced in the animal diet with adequate calcium (Ca) and vitamin D_3 for growth, lactation, gestation, reproduction, and lactation. Deficiency of P is the most widespread of all the mineral deficiencies affecting livestock Calcium and P imbalances associated disorders such as post parturient haemoglobinuria, pica, rickets, osteomalacia, fibrous osteodystrophy (due to primary or secondary hyperparathyroidism) and urolithiasis are well-recognized problems in ruminants. Supplemented inorganic P not used by the animal is primarily excreted in faeces, a potential source of environment pollution. Serious measures should be adopted to reduce P excretion in livestock.

Keywords: *Phosphorus; Ruminants; Biological Role; Bone Disorders; Reproductive Disorders*

Introduction

Calcium (99%) along with Phosphorus (80%) provide the bulk of the bone tissue giving it strength. The physiological role of Ca and P in animals is well established. Calcium and P levels in cows (8.4 - 11 mg/dl; 4.3 - 7.8 mg/dl), goat (9 - 11.6 mg/dl; 2.3 - 5.6 mg/dl), sheep (9.3 - 11.7; 3.7 - 9.7 mg/dl),and dromedary camel (8 mg/dl; 4 - 4.5 mg/dl) as stated by Damir [1]. Phosphorus (P) is one of the essential macrominerals needed for various body functions. It is needed in adequate quantities to optimize performance of ruminants It has many functions in energy metabolism, as phospholipids in membranes, as part of RNA and DNA, in enzymatic activities, in acid-base balance, bone mineralization, cell signaling and buffering systems. Phosphorus constitutes 1% of the total body weight, 85% of it is found in the

body skeleton, 15% in blood and soft tissues and (0.1%) in extracellular fluid. Phosphorus is highly reactive and found as phosphate in nature. Phosphates are found either as highly water-soluble inorganic compounds or as organic compounds bound to lipid, amino acid or carbohydrate. Normal serum P_i concentrations range is 4 - 8 mg/dl (1.3 - 2.6 mmol/L) for ruminants [2].

Salivary phosphorus

For any given diet, P output in saliva is dependent on P intake and mostly in the form of inorganic phosphate. In cattle rumination is the most effective stimulus of saliva secretion. The salivary glands actively concentrate P_i (370 - 720 mg/L) obtained from blood as stated by and salivary P concentrations are always far higher than plasma concentration (between 4 - 15 mmol/L in saliva compared to 1 - 3 mmol/L in blood plasma). The daily output of salivary P remains constant because its concentration in saliva is directly proportional to plasma P concentration and inversely related to saliva flow rate. Valk., *et al*. [3] studies nourished the findings that a direct relationship between blood and saliva P concentrations exists but with some variations. Some regulatory factors and measurement methodology dissimilarities were considered to be the cause of variations and making the statement contradictory. Increased PTH levels also stimulate P secretion in the salivary glands and a decrease in salivary HCO^{3-}, as the sum of [HCO^{3-}], [HPO_4^{2-}] and [Cl^-] remains fairly constant (and equal to the sum of [K^+]) and [Na^+] in saliva). In cases of severe P deficiency and hypophosphatemia role of PTH somehow remains invalid and could not exert the same effect on salivary P secretion. Moreover, Maekawa., *et al*. [4] stated that roughage (40 - 60% of DM) intake has no influence on total daily saliva production in dairy cattle at equal DMI. The calculation of total saliva production was based on feeding time, rumination time and time for rest in animals for 24hrs. multiplied by the respective rates of saliva production as measured by saliva collection and feed boluses collected from inside rumen. For higher levels of roughage, long eating and rumination time related to higher rates of saliva production, but equal total saliva production on daily basis was maintained by lower saliva production during rest time. Inorganic phosphorus ($P_{i)}$ concentrations in ruminal fluid is determined predominantly by the extent of salivary P secretion [5]. This salivary P is utilized by the ruminal microflora and after outflowing to the intestine reabsorbed again along the gastrointestinal tract, as efficiently as dietary P. This P recycling provides both a buffer mechanism to the rumen contents and a highly available P source for rumen microflora multiplication and metabolism. In the absence of significant fluxes of this essential mineral across the rumen wall, the only sources available in the rumen are feed and saliva, and thus the salivary P_i is the most important.

Nutrition of ruminal microflora

Phosphorus is an essential macro-mineral for rumen microbes. Thus, the GIT microbes have a requirement for P which is distinct from the requirements of cattle. In rumen the concentration of available P must be sufficient to rumen microflora requirements to prevent any constraint on rumen fermentation. When P_i concentration is less than 50 - 80 mg/l, then the activity of ruminal and caeco colic microbes is likely to be minimized due to a reduction in breakdown of cellulose and hemicellulose. Van Straalen and Bruinenberg [6] studied that a minimal ruminal P concentration of 2 - 3 mmol P/l is necessary for optimal microbial and cellulolytic activity and base their presumption on previous *in vitro* studies The studies on *in vitro* rumen incubations concluded that microbes fermentation rate is reduced at concentrations < 0.5 mmol P/L. A study by Sevilla [7] suggest that ruminal P_i levels in ruminants are rarely below 200 mg/l, although lower levels may be found in the colon. Furthermore, Bannink., *et al*. [8] also supported this with three arguments. Firstly, saliva contribution to rumen fluid is about 3 times the volume of drinking water; rumen P concentration therefore closely match to that of saliva. Salivary P content depends on plasma P concentration but stays at relatively high levels at even reduced dietary intake (2.4 g/kg DM), Secondly, microbial multiplication requires a maximum of 70 g P/d, which is easily met with feed intake and saliva production. Finally, a dietary P level below 2.4 g P/kg DM is very hard to achieve even with common roughage-based diet because saliva P concentration does not drop below 5 mmol/l, the last argument is also strengthened by studies conducted by Valk., *et al* [3]. In contrast, Van Straalen., *et al*. [6] observed a rather high P requirement for optimal microbial cellulolytic activity for 7.7 g/kg fermentable organic matter. It seems likely that P concentration in rumen (2 - 3 mmol P/l) can easily be met by saliva production which seldom contains P less than 5 mmol/l. In practical situations animals with sufficient rumination activity it's very unlikely to have P deficiency at rumen level. On a diet containing P about 25% below the recommended level (2.4 g P/kg DM) rumen P concentration remains around 3 mmol/l, which appears to be still adequate for

fermentation. The general conclusion is that the levels of P found in the rumeno-reticulum are generally adequate for optimal microbial activity even with highly P-deficient diets.

Phosphorus absorption

In ruminants water soluble P_i sources are available for absorption, while the solubility of organic phosphorus (P_o) depends upon the ability of the animal to convert organic into soluble inorganic form or more acceptable organic form [9]. In ruminants, microbes secrete phytase enzymes which hydrolyzed the dietary phytate P and release P_i. The P_o which is not hydrolyzed in the rumen becomes soluble in abomasum at low pH. The dietary calcium (Ca) level is considered to have little effect upon the absorption of P if dietary P levels are adequate. The desirable Ca to P ratio has for a long time been defined as lying between 1:1 and 2:1 due to the Ca to P ratio of bones. However Ral studies suggest that the Ca:P ratio becomes critical if it is greater than 7:1 or less than 1:1 [10].

Animals fed on P deficient diets with high levels of Ca may suffer reduced P absorption due to reduction in rumen P solubility and also a reduction in availability of dietary P at sites further down the small intestine. Therefore, it seems likely that ruminants can tolerate a wide range of Ca:P ratios as long as the dietary supply of each mineral is adequate and their vitamin D status is also adequate. Absorption of P from the rumen and omasum is insignificant and it has not been clearly demonstrated that P is absorbed from the abomasum. Small intestine is the main site where P absorption takes place and its transport occurs via both active and passive diffusion. Passive Diffusion takes place or when P concentration in the digesta is very high, especially in the jejunum part of GIT; at low P concentration, active transport takes place by NaPI co-transporters, especially in the first and middle part of the small intestine as shown by gene-expression of different intestinal sections in dairy cows. Insignificant quantity of P is absorbed from the large intestine. In contrast, sheep colon has the capacity to absorb significant quantities of phosphorus. In young, growing calves, intestinal absorption is higher than in older cattle. Serum levels of P_i are also higher in calves (presumably to provide sufficient quantity of P_i for the higher level of bone mineralization. Factors which may interfere and minimize the absorption coefficient of P are parasitic infestations and P- mineral interactions. Minerals such as Ca, Fe, Mg, Zn, Mn. K, Al and Mo, form insoluble and unabsorbable complexes with P that reduce the absorption process in animals.

Phosphorus excretion

In adult cattle daily loss of P is less than 2 mg/kg or less than 1g per day. The kidneys act by filtering off a part of fluids in the blood and consequently essential nutrients including P are reabsorbed and are retained by the body. Urinary phosphorus is the alternate phosphorus excretion pathway in the ruminant although; it is quantitatively negligible [11]. In growing calves urinary phosphorus could represent as much as 0.88 of the total phosphorus loss [12]. In sheep urinary phosphorus excretion might be genetically predetermined [13]. Urinary phosphorus excretion contributes to phosphorus homeostasis of sheep and can be stated as a fixed phosphorus loss (Braithwaite, 1980). By decreasing the glomerular filtration rate, the animal can adjust the plasma phosphorus (Bijvoet, 1976) and excrete extra phosphorus when plasma increases above a plasma phosphorus concentration threshold close to 2 mmol L^{-1}, 1.6 mmol L^{-1} (cattle), 2 mmol L^{-1} (calves), 2.6 mmolL^{-1} (ruminants) and 2 - 3 mmolL^{-1} (calves) as stated by Bravo., *et al*. (2003). A study in small ruminants has shown that when the level of plasma P_i is above 6 mg/dl the reabsorption capacity of the kidney tubules is exceeded and significant amount of P is lost in the urine. The type of the diet also affects urinary losses of P in dairy animals. When dairy cattle fed concentrate diets, considerably more P is excreted in urine; this is largely due to the low rate of saliva secretion and because of P rich diets. In small ruminants and many other species the excess of inorganic phosphate formed are excreted from the body in urine via the kidneys during first two weeks of their life. In adult ruminants almost all P excretion occur through faeces [13]. This is a major difference in excretory process between ruminants and non-ruminants and is due to a greater ability of the ruminant kidney to reabsorb phosphate. In the non lactating ruminants, the faeces are the major route for the excretion of P [14]. Recently, Alvarez-Fuentes., *et al*. [15] concluded that on average, lactating dairy cows excreted 58% of ingested P in faeces, 0.44% in urine, and secreted 40% in milk. Furthermore, at constant dietary P intake, cows with higher milk production excreted less P as compared to cows with lower milk production. The P content of milk is independent of dietary P intake and remains relatively constant and thus a major source of loss of endogenous P. Generally, fecal excretion of P contains three fraction 1)

Dietary P that is not available for absorption (unavailable P) 2) Available dietary P that was not absorbed 3) Endogenous P from all, but primarily salivary sources. The latter two are present in the rumen as P_i and are considered to be undifferentiated as they pass through the intestine, Hence, they have the same coefficient of absorption. Organic P excretion remains relatively constant and independent of the amount of P ingested, whereas fecal inorganic P varies directly with P intake. Thus, the study of P and efficiency of its utilization in ruminants is not simple because of substantial amount of P is secreted in the saliva endogenously which sometimes surpasses the total amount of endogenous P excreted in faeces and urine.

Phosphorus requirements

Phosphorus requirements for dairy animals are calculated as the sum of the P retained by the animal, P lost in animal milk and conceptus and endogenous P losses in faeces and urine. This value is adjusted for the availability of dietary P. During body growth P retention is estimated from data on the P content of animals at various physiological states. The 1989 NRC requirements for P are 10% to 22% higher than the previous recommendations due to lowering of the assumed absorption efficiency in animals. According to NRC [16] the estimated P requirement is about 3.2 g/Kg DM for dairy cattle and 3 g/Kg DM for dairy goats. Similarly, P requirement in dairy sheep is 0.16 - 0.38 (mg/kg DM of diet [17]. According to German standards (GfE, 2003) P requirements for dairy cattle are 32 g/d and for growing cattle 6.6 - 7.5 g/d Comparisons are also made for lactating camels. The recommendations for cattle producing 10 kg milk are used as a comparison for camels, although camels produce less milk. It is important to remember that daily P requirements are for grams of P not P as % of the ration dry matter (DM). Rations should be formulated based on the grams of P required rather than as a % of DM.

Homeostasis of phosphorus and calcium

Vitamin D3

Hypophosphatemia and increased levels of PTH induce Vitamin D3 production in ruminants. An alternative regulatory circuit for intestinal P uptake also exists that is up-regulated independently even in absence of vitamin D3 in states of hypophosphatemia [4]. Vitamin D3 is produced by the kidneys and is the main regulator of active intestinal absorption of Ca and P, stimulating P uptake in the small intestine by activating NaPI transporters. It also increases renal reabsorption of P by increased NaPI transporter activity in the kidneys.

PTH

The parathyroid glands directly respond to changes in serum Ca by a Ca-sensing receptor, resulting in increased PTH production. It is not directly responsive to intravenous P infusion but indirectly responds to extracellular P concentrations by its effect on mRNA stability coding for PTH synthesis which destabilizes in cases of hypophosphatemia [18]. Once released in the circulation, PTH affects the renal excretion of P by reducing tubular reabsorption through internalization of the NaPI transporters, thus increasing urinary P concentration. Additionally, PTH stimulates bone turnover and Ca and P flux from the skeleton and increases vitamin D3 production. It also stimulates active P secretion in the salivary glands.

Calcitonin

Calcitonin is also produced in the parathyroid glands, and mainly involved in Ca balance. With the current state of knowledge its direct role in P homeostasis is moderate. However, calcitonin is found to increase and decrease with high and low extracellular P concentrations, respectively, leading to a lower and higher bone resorption [19].

Phosphatonins

Parallel to calcitonin reducing serum Ca, a group of substances for P regulation has been named 'phosphatonins' based on their effect on decreasing serum P levels. Fibroblast growth factor 23 (FGF-23) and secreted frizzled-related protein 4 (sFRP-4) are the most relevant factors in this group, reducing P balance by increasing renal excretion and reducing vitamin D3 synthesis while leaving Ca balance unaffected. FGF23 expression can be stimulated by vitamin D3 as well as PTH activity [20]. Fibroblast growth factor 7 (FGF-7) and matrix

extracellular phosphoglycoprotein (MEPE) also reduce reabsorption of P from urine, but their effect is compensated by increased vitamin D3 activity.

Phosphorus and milk composition and production

Underwood [21] stated that P deficiency reduces milk yield but does not affect composition of milk. Therefore, P supplementation could be expected to increase milk production in a P deficient situation in dairy animals. Various studies (recorded increases in milk yield when P supplements were fed to the dairy cows grazing on grass-legume pastures. Contrarily, Holroyd., *et al.* [22] reported the results of the study conducted for full three years and showed insignificant effect of P supplementation on milk yields during the first three lactations in dairy animals. In milk, about 70% of P is in inorganic form and 30% in organic form. In milk about 70% of calcium and 50% of P_i is located in the casein micelles, preventing precipitation of calcium phosphate and providing micelles with structural stability [23]. The ratio between milk casein and milk P is rather constant, providing a physiological foundation for a fragmentary relationship between milk protein content and milk P content. Milk serum supersaturation with calcium phosphate, indicates that increase in P_i concentration in milk is mainly related to increases in casein content, and thus increasing P_i secretion capacity. Inorganic P secretion is related to synthesis of and lactose and casein in the Golgi complex and endoplasmic reticulum. This physiological background of P_i, milk casein and lactose synthesis pathway was confirmed by the fact that significant correlations could be established between milk lactose protein and milk P content.

Regulation of phosphorus in bones

In animals about 80-85% of total body P is present in bones within a collagen matrix in the form of hydroxyapatite. Net accretion of P in growing animals is in bones, while in case of hypophosphatemia in early lactation in dairy cows' bones can provide an extra contribution equal to 15 - 25% of daily P intake by resorption of P from bone reserves [2]. This indicates that bone P has an intense impact on animal P balance, in the regulation of blood P concentration, in milk P secretion and specifically in P recycling for rumen P availability for rumen microbes. Turnover have shown variations in bones in different anatomical locations, having structure dissimilarities depending on their function. Weight-bearing bones of the limbs are longer and much heavier and more resistant to breaking than for example the tail (caudal) vertebrae. Bones with high fraction of trabecular over cortical bone are therefore most relevant in cow P metabolism, with porosity facilitating the exchange of P_i between bone and the rest of the body. At severe P deficiency long bones start to show loss of minerals. In sheep cancellous bones have been much more affected. Bone mineral accretion and resorption are mediated by two cell types: calcification promoting osteoblasts in bone formation; and osteoclasts, demineralizing of bones by osteoclasts. The reduction of bone mineral content in early lactation has commonly been described as a natural process in many mammal species. In small ruminants, bone mineralization decreases during early lactation while after mid-lactation, mineralization increases again. Bone metabolism is regulated by both PTH and 1,25-dihydroxyvitamin D3 Hypocalcemia induces PTH secretion. Thus, onset of lactation around parturition causes a decrease of plasma Ca, thereby increasing PTH secretion. PTH will increase vitamin D3 activation in the kidneys and both will stimulate bone resorption, releasing Ca and phosphorus. In mammals during pregnancy, plasma calcitriol is increased even without any dietary Ca deficiency or any increase in PTH level. Calcitonin levels also increases due to its production in the mammary gland, placenta and thyroid gland. PTHrP is produced in the developing mammary gland and placenta, stimulating bone mineralization in the fetus [24]. Renal activation of vitamin D3 is directly stimulated by prolactin or placental lactogen like pregnancy factors. In the absence of calcitriol, placental lactogen and prolactin are involved directly in increasing intestinal calcium absorption. All these factors activate bone metabolism and increase bone resorption, as shown by increased levels of bone resorption markers, especially increases during the third trimester which coincides with the largest mineral accretion of the growing fetus. In dairy cows, older cows are more prone to hypophosphatemia and hypocalcemia than heifers. Heifers produce less milk and have therefore lower P and Ca outputs; with more active bone metabolism, giving easier accessibility to bone reserves, during their growing period as indicated by higher blood osteocalcin concentrations. Demineralization of bone, releasing Ca and P_i is facilitated by acidogenic diet. As reported in a condition of metabolic acidosis caused by rumen acidosis may do the same in ruminants. Dietary P concentration below requirements (2.3 g P/kg DM during lactation) decreased milk yield feed intake, P_i

concentration in plasma and increased the bone marker CTX for resorption [25]. Bone mineralization and even bone strength is markedly affected by low P intake. At dietary P levels of 0.31% relative to 0.39% or 0.47%, total ash and P content tended to be lower in rib bone sections of dairy cattle; but bone strength was not significantly affected [26]. Studies that do find reduction in bone strength is closely associated with severe mineral deficiencies but do not show a linear effect of P supplementation on bone strength Incidence of Milk Fever (hypocalcemia) due to low levels of dietary Ca in early lactation promotes hypophosphatemia through PTH release. At hypocalcemia, PTH is secreted to mobilize Ca from bones. Another effect of PTH is to increase P excretion in saliva and urine, thereby increasing P losses and decreasing plasma P_i. Mineral-rich feed intake and prevention of Ca deficiency are therefore vital to prevent losses of P.

Phosphorus imbalances in ruminants

Underwood (1966) stated that 'there is no doubt that P deficiency is the most widespread and economically important of all the mineral disabilities affecting grazing livestock'. Following are important disorders related to imbalances in dietary P in ruminants.

Reproductive disorders

There has been much debate and research conducted on P supplementation effects on reproductive functions. Decreased fertility rate, irregular estrous cycles decreased ovarian activity, delayed sexual maturity, increased occurrence of cystic ovaries, and low conception rates were observed when P intakes are low. In a field study heifers with hypophosphatemia showed reduced fertility with 3.7 services per conception. Services per conception were reduced to 1.3 after adequate P was supplemented. In another study, increasing P supplementation of the ration gradually from 0.4% to 0.6% had no significant effect on days to first estrus or services per conception. However, in some instances, significant difference in responses have been reported in the field when P supplementation was increased gradually to 0.5% or 0.6%.The reason for these variations in response is unclear, but may be related to the availability of the P that is added to the ration or the actual amount of P consumed in the diet [27].

Similarly, breeding cattle grazing in a P deficient situation have poor reproduction rates. As a result, it has been suggested that *per se* deficiency has a specific effect on reproduction rates in cows. There are reports in literature (that provision of supplementary P can increase pregnancy rates, it is not possible to partition the amount of response due to increased P intake *per se* and that due to the increased feed intake which normally accompanies the correction of a P deficiency.

Rickets (Rachitis)

It is a disease of lambs, calves, foals which is characterized by a failure of growing bone calcification or to harden, properly. The condition is characterized as a uniform widening of the epiphyseal diaphyseal cartilage and an excessive amount of osteoid or non-calcified tissue, causing enlargement of the ends of long bones and the costochondral junction of the ribs. Symptoms that often precede the more severe clinical manifestations are loss of appetite, slow growth rate, digestive disturbances, tetany. The calves are reluctant to stand due to stiffness and lameness. There is enlargement of joints and costochondral junctions with curved long bones producing 'rachitic rosary' and "bow-legged" like condition in animals. Teeth show poor calcification and pitted with dental malocclusions. Either hypocalcemia or hypophosphatemia or both are usually observed in this condition. At post-mortem examination the bone cortices are wider and softer than normal with enlarged joints, the long bones in particular, show lateral or medial deviation. The increased width of the epiphyseal plate, which is the hallmark of rickets, is visible grossly. Successful treatment of rickets depends on supplying adequate amounts of vitamin D and adjusting the intake and the ratio of Ca and P.

Osteomalacia or adult rickets/osteoporosis/osteoporosis

Three abnormal bone conditions are characterized by alterations in the conformation of the skeleton. Several factors including P or Ca deficiency, an abnormal proportion of Ca and P in the ration, altered rate of secretion of certain endocrine glands such as parathyroids, and Vitamin D deficiency are involved in production of these changes. A coexisting vitamin A and protein deficiency may also be involved

in some cases. According to Underwood and Suttle [9] highly leached and iron-rich acid soils are particularly unlikely to provide adequate P and dry weather aggravate the condition.

Osteomalacia is a disease of adult animals with characteristic symptoms of softening and replacement of bone with osteoid tissue, which resembles uncalcified bone. The disease is common in pregnant or lactating cows on P deficient diets. Calcium and vitamin D deficiency may also be involved. Osteoporosis is a faulty bone metabolism characterized by porous structure, atrophy and failure of normal bone mineralization. Osteoporosis is a condition where bone is partially replaced by the soft poorly calcified fibrous tissue. Caprine are also affected with similar condition. The animals are easily fatigued, with snuffling respiration, and signs of lameness. The above conditions can be cured and prevented 1) By using natural feeds that contain sufficient quantities of calcium and phosphorus (wheat bran, whole cereal grains, cottonseed, linseed, peanut and soybean meals etc.) 2) By fertilizing the soils on which the crops are grown 3) By feeding a specific mineral supplement e.g. phosphate lime stone, di-calcium phosphatidic-sodium phosphate.

Pica

Pica is a depraved or abnormal appetite, it is usually associated with animals that chew or eat fences, dirt, trees, bones, wood or other inanimate objects not usually considered normal feedstuffs [9]. It has been associated with unequal dietary calcium-phosphorus ratio and P deficiency [28]. Serious complications of pica include cannibalism, penetration of foreign bodies in the alimentary tract as traumatic reticuloperitonitis, botulism, or accumulation of wool, fiber (fibrolite) or sand and may cause obstruction of digestive tract [28]. The condition is found in pregnant and lactating dairy cattle, buffaloes and in small ruminants. Several reported indicated a significant decrease in serum P concentration in calves having earth eating behavior. Several studies indicated that circulating P_i levels were significantly lower in the animals with pica than in healthy controls in camels, cattle and buffaloes. It is primarily a mineral deficiency condition adjusted with supplementation of good mineral mixtures.

Postparturient hemoglobinuria

For the first time hemoglobinuria was reported in Scottish cattle following parturition. Similar descriptions of the condition from various countries under a variety of different names is quoted in literature. Parturient hemoglobinemia or hemoglobinuria, Red water and Nutritional hemoglobinuria. have been used synonymously with post parturient hemoglobinuria which is the description favored in many publications is a sporadic metabolic condition of multiparous high producing dairy cattle characterized by anemia, intravascular hemolysis, and hemoglobinuria. A disease with many similarities has been described in sheep, Egyptian and Indian buffaloes and caprine.

It has been postulated that P deficiency was a necessary predisposing factor and feeding cruciferous plants (*Brassica*) precipitated the hemolytic crisis. Since 1930s the list of feeds associated with post parturient hemoglobinuria has expanded to include, green oats, sugar beet roots and leaves, Egyptian clover, alfalfa and members of genus *Brassica*. In addition to the low P content (< 0.4% dry matter) or high calcium to P ratio (> 2:1) in the above-mentioned fodders, certain hemolytic substances (found in rape, sugar beet and kale) may interact with a low serum P concentration to produce this periparturient metabolic condition. A report indicates that affected dairy animals suffer pregnancy stress from the seventh month of pregnancy and have a significant wider ratio of blood Ca:P compared to the earlier stages of pregnancy. Another study reported that very low levels of serum P were observed in crossbred and non-descript cattle. The first sign of disease is seen 20 ± 10 days, before or after parturition when affected animals pass red to coffee colored urine. Other associated clinical signs are anemia, jaundice, recumbency, labored breathing and inappetence [29]. Similarly, treatment of hemoglobinuria with sodium acid phosphate (20% solution) administered simultaneously by i.v. or s.c and oral routes resulted in, almost 100% recovery of affected animals within 1-3 days. Intravenous infusion of sodium acid-phosphate (60g in 300 ml of water), and 100g of bone meal administered as a drench twice a day and correction of any P deficiency or imbalance in the ration also resulted in complete recovery of the dairy cattle [28].

Urolithiasis

In ruminants urolithiasis affects both sexes, but urinary blockade is a major problem only in males. The species-wise incidence has been reported as goats 49.83%, cattle 32.87% and sheep 1.04%. The condition may occur due to excessive or imbalanced intake of minerals. In feedlots ration high in cereal grain and oil meals provide high levels of P and Mg but relatively low levels of Ca and K that predisposes disease condition. A calcium-phosphorus imbalance results in high urinary phosphate excretion which is an important factor in the genesis of phosphate calculi. The sigmoid flexure is a common site for urolith to lodge in all ruminant species. In small ruminants the urethral process is an extremely common site for uroliths to lodge [30]. In ruminants struvite uroliths (magnesium, ammonium or phosphorus) occur due to high grain feeding and low dietary Ca to P ratio. In ruminants silica urolithiasis is associated with high dietary Ca to P ratio. For prevention of the condition Ca to P ratio of 2:1 should be provided in the ration. Alfalfa and grain feeding should be eliminated or reduced and changed to grass hay as primary forage to reduce urinary load of calculogenic minerals.

Fibrous osteodystrophy

Fibrous osteodystrophy is a metabolic disorder characterized by extensive bone resorption, insufficient mineralization of the bone tissues and proliferation of fibrous connective tissues. The persistent increase in the plasma parathormone (PTH) levels, may be associated with primary (rare in domestic animals) or secondary hyperparathyroidism in ruminants. Nutritional or secondary hyperparathyroidism usually affects young animals fed diets with low calcium and relatively high phosphorus contents. The condition includes decreased concentration of serum ionized calcium and consequent increased synthesis and secretion of PTH. The main clinical signs include bone deformities and enlargements, increased susceptibility to fractures, and mobility or postural disturbances. Disease is sporadically described in goats, however, it is rare in sheep and cattle [31].

Phosphorus biomarkers

Blood

Inorganic phosphorus concentration in adult dairy animals ranges from 1.4-2.6 mmol/L with an average 1.5mmol/L and 1.9 to 2,6 mmol/ L in growing animals. Preanalytical factors serum vs plasma, jugular vein vs coccygeal vein, timing of sampling facing vs after meal effect the P_i concentration in blood. Blood samples from jugular vein have 4-9% lower P_i as compared to blood samples from udder vein or tail vein, due to extraction of P_i in the saliva. Similarly, if NaF is used as a coagulant it may reduce P_i by 10% relative to the use of vacutainers or heparin. Generally, young animals have higher serum P_i for bone mineralization. Serum P_i is an indicator of non-bone, extracellular P status in animals. However, about 90% of non-bone P is present intracellular. Therefore, blood P concentration is not a good representative of total P status of dairy animals. Furthermore, changes in intracellular and extracellular P balance can occur suddenly thus complicating the P status in instantaneous blood test as described by Grunberg., *et al* [32]. They observed hypophosphatemia in animals fed on P deficient diet (1.8g P/Kg DM) initially for few days then increase in P concentration after ± 9 days without clinical signs of P deficiency. There are two major difficulties with plasma P_i estimation 1) When P is not primary limiting mineral and its concentration is at or above normal levels. Under certain conditions protein and P deficiencies occur simultaneously. In those specific situations feed intake and body weight is reduced and plasma P_i level increased by bone resorption. A significant relationship between feed intake and plasma P was observed when dietary crude protein was included as additional variable 2) Dehydration, excitement and stress may complicate the results. Serum P_i concentration is not a good indicator of P balance in bones. In ewes fed on P deficient diet (1.5g P/d), a low serum P_i concentration and bone resorption was detected. When P was supplemented in diet (4.5 g/d), blood P_i increased within one month with inadequate bone mineralization. So in chronic P deficiency blood plasma P_i is a poor indicator of P status. Red blood cells may be used to estimate P_i and intracellular P concentration in animals. Severe hypophosphatemia induce RBC lysis due to insufficient ATP to maintain membrane stability in erythrocytes. Hypophosphatemia along with other factors results in hemolysis or a change in osmotic resistance or P_i contents of RBCs. As an alternative, Ca levels in blood in conjunction with P can be monitored. But it requires further probing to what extent Ca:P ratio is constant during bone resorption, variation in P status in animals and interference of homeostatic regulation mechanism.

Milk

In milk 70% P is in inorganic and 30% P is in organic form. About 50% of P_i is in casein micelles, maintaining structural stability and calcium phosphate precipitation [23]. Total milk P concentration ranges from 0.7-1.2 gP/kg milk between individual cows [5]. Wu., *et al.* [26] stated that a partial relationship between milk protein content and milk P content can be established by constant ratio between P and casein. Milk P variation can be effected by cow parity, stage of lactation and genetic factors. In a study Peterson., *et al.* [33] found negative relationship between dry cow P supply in diet (2.1, 3.1 or 4.1g P/kg DM) and postpartum milk P concentration during first four weeks after calving.

Fat-soluble vitamin D_3 concentration vary irrespective of P balance due to difference in grazing seasons and variation in duration of sunlight exposure [34]. PTH-related peptide (PTHrP) can be detected in milk and serum. It is produced in the udder in response to local factors such as calcitonin, prolactin, sucking, and P and Ca receptors [24]. The role of PTHrP in mineral metabolism during lactation is still unclear.

Bone

Representative bone biopsies in animals give an indication of long term P balance. Bone seems to respond slowly to actual P balance by either increasing demineralization (osteoclast activity) or calcification (osteoblast activity), which varies over time depending on P requirements. So instantaneous bone sample for P content cannot be used as a marker for changes in animal P pool. During bone resorption collagen is also degraded. Serum carboxyterminal telopeptide of type 1 collagen detected as bone resorption marker. Two collagen breakdown products Pyridinoline and deoxypyridinoline can be found in urine, deoxypyridinoline (DPD) being the most specific for bone collagen content breakdown. The ratio of DPD to creatinine concentration in urine may help to determine bone resorption in dairy animals after feeding P (0.18%) for four days in diet [32]. The significance of biomarkers to determine P status in dairy animals need further investigations.

Saliva and ruminal fluid

The concentration of P_i in saliva depends on total saliva production in P_i concentration in plasma. It is never below 5 mmol/L even in P deficient diet (2.4 g/kg DM) as mentioned by. Taking representative digesta free saliva samples for P_i determination in salivary glands is a very complicated process. Moreover, salivary P_i production vary according to the variation in salivary glands.

In ruminants ruminal fluid P_i concentration does not provide additional information on body P pool. The P_i level in ruminal fluid depends on dietary, blood P and saliva production. Whenever there is decrease in dietary P, salivary P_i is stimulated that prevents P reduction in ruminal fluid in ruminants [2].

Urine and faeces

In adult ruminants P_i concentration in urine is very low and is not representative of body P status. Urinary deoxypyridinoline is a useful indicator to determine Ca and P balance and bone resorption. Fecal P is the most important route for P excretion from animal's body next to milk synthesis. It also indicates P balance presuming the accurate estimation of feces produced (Kg feces/d x gP/kg feces = g P/d). The amount of P excreted and the chemical form in which P is excreted (inorganic or organic form) depends on dietary P content. Inorganic P excretion increased with increased P allowance. Fecal P excretion considered as an indicator of body P status, about 2g P/kg fecal DM indicates adequate P level and higher values indicate excess P feeding in animals. Although there is a good correlation between P intakes with feed and total P excreted with feces. Still extensive studies are needed to assess accuracy and reliability of this method.

Tissue biopsies

By taking liver and muscle tissue biopsies, intracellular status of P can be analyzed. In case of deficiency, bone resorption compensate resulting in relatively constant tissue P concentration. During short term P deficient diet (1.8g P/kg DM), muscle P content was constant and within normal reference range, while electromyography diagnosed subclinical muscle dysfunction [32].

Environmental Pollution

Globally there is increase in public concern about environmental pollution by excessive use of P by livestock production systems. If scientific findings are generalized < 40% of P is utilized by the animal depending on its availability, feed conversion efficiency and amount of mineral consumed in excess of the body requirements. Thus large amount of P is excreted in feces by the ruminants. Moreover, P_i is a finite resource and needs wise strategic approach in its usage. Inorganic P supplementation if not utilized adequately by the animal is excreted in feces that leads to its accumulation in soil, leaching of groundwater or eutrophication of surface water due to P transport in runoff. Accurate calculation of animals requirements and feeding them in groups made according to the similar physiological status and P requirements can help in reduction of environmental pollution. Moreover, use of phytase enzyme to improve digestibility of dietary phytate content will serve the purpose. Finally, rotational grazing in overfertilized pastures may help to reduce P runoff [35-52].

Conclusion

In ruminants majority of phosphorus is found within the teeth and bones. Phosphorus is a requisite in almost all metabolic functions and energy transfer mechanisms within the body. It must be provided in adequate amounts in dairy animals for their optimal growth rates, improving feed efficiency, augmentation of milk production, and increasing reproductive efficiency. Furthermore, ruminants have developed high salivary P, secretion mechanism in order to maintain rumen microbial metabolic activity as long as possible independent from dietary P supply. Over supplementation of P in livestock does not improve milk production or reproductive performance. Extensive research on P based feed management plans for livestock is needed to minimize the excessive amount of phosphorus excreted as manure and to protect the environment.

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