Vitamin D Rickets: Diagnosis, Treatment and Prevention

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Abnormal bone growth is a commonly diagnosed problem in young growing animals of all domestic species and is usually related to nutritional deficiencies. A rickets syndrome in juvenile llamas and alpacas characterized by a shifting leg lameness and enlargement of the joints, most noticeably the carpus, has been described. Affected crias have variably shown a slowed growth rate, reluctance to move, and kyphosis. Radiographic evidence of physeal ectasia and low serum phosphorus concentrations were consistent with a diagnosis of rickets. The Camelid Research Group at Oregon State University had investigated the role of vitamin D in hypophosphatemic rickets over a period from 1993 to 1999. Our initial involvement in this activity was the result of an inquiry from Dr. Pat Long who was not convinced that phosphorus supplementation was correcting the identified problem. Since our initial study we have completed 4 additional studies dealing with various aspects of etiology, treatment, and prevention of this syndrome. The following are summaries of the pertinent findings from these studies.

Study 1: Role of Vitamin D

In our first study we defined the role of vitamin D in the hypophosphatemic rickets syndrome. Twenty clinically affected and 10 age and sex matched non-clinical control llamas and alpacas from 9 farms were compared (Van Saun et al. 1996). While serum calcium (Ca) concentrations did not differ between clinical and non-clinical groups, serum phosphorus (P) concentrations in the control group (9.0 ± 0.9 mg/dl) were higher than in the clinical group (3.4 ± 0.2 mg/dl). This was consistent with the original disease syndrome description by Fowler. Serum vitamin D (25-hydroxy vitamin D) concentrations in the control and clinical groups, 83.2 ± 20.2 nmol/l and 7.4 ± 1.9 nmol/l respectively, differed supporting the hypothesis that insufficient vitamin D_3 production played an important role in the development of rickets in the llama and alpaca. Vitamin D concentrations and month of birth accounted for nearly 60% of the variation in serum P concentrations.

Another aspect of this study was showing that vitamin D supplementation alone could improve phosphorus status. Ten clinical animals were subsequently treated with either parenteral or oral gel forms of vitamin D. Calcium, phosphorus and vitamin D concentrations were measured before and after treatment. The data in Table 1 show significant increases in both P and vitamin D concentrations with treatment. These results then set the stage for subsequent studies determining an appropriate treatment and prevention protocols.

Study Conclusions: Vitamin D deficiency induces low serum phosphorus concentration in growing llamas and alpacas resulting in a hypophosphatemic syndrome. Supplementation of vitamin D can increase both vitamin D and phosphorus status.

Table 1. Mean serum concentrations of calcium, phosphorus, and vitamin D in paired samples obtained from 10 rickets-affected camelids before and after treatment with a vitamin D supplement.

Serum Parameter	Time Relative to Treatment		
	Before	**After**	**Reference**
Calcium, mg/dl	9.7 ± 0.26	10.1 ± 0.22	8.4 – 10.8
Phosphorus, mg/dl	3.6 ± 0.40	8.9 ± 0.49	5.1 – 9.0
Vitamin D, nmol/l	5.9 ± 1.4	259.9 ± 53.6	> 75
Vitamin D, ng/ml	2.4 ± 0.6	104.0 ± 21.4	> 25

Reference: Van Saun, RJ, Smith, BB, Watrous, BJ. Evaluation of vitamin D status in llamas and alpacas with hypophosphatemic rickets. **JAVMA** 1996;209:1128-1133.

Study 2: Seasonality Effects

Both owners and veterinarians reported a seasonal incidence of this problem with cases being diagnosed primarily between November and March in the northern hemisphere. This observation fits well with the finding of low vitamin D as the causative agent. Vitamin D requirements of the animal are met by either dietary supplementation or synthesis in the skin by the animal. We hypothesized that insufficient sunlight during the winter months resulted in decreased vitamin D production by the animal. This is not a unique situation to llamas, but has been documented in sheep in both northern and southern hemispheres during winter and summer seasons, respectively.

In study 2, serum Ca, P, and vitamin D concentrations in 30 llamas and alpacas were measured at monthly intervals for 12 months (Smith and Van Saun, 2001). Analysis of samples collected from 13 of these llamas (5 juveniles, 4 teenagers, and 4 adults) for 12 months showed no seasonal change in serum Ca concentrations. In contrast, P and vitamin D concentrations declined significantly during the winter months. Highest vitamin D concentrations were seen through the summer months peaking in September. An interesting secondary finding was that vitamin D concentrations increased following shearing. This observation would suggest that the fleece blocks out much of the sun's rays. Similarly, we found that coat color also impacts potential for vitamin D synthesis. Two jet black alpacas never showed any increase in serum vitamin D concentration compared to white or cream coated individuals. The severity of the decline in vitamin D concentrations was most pronounced in the youngest animals with mean P and vitamin D concentrations decreasing to 50% and 10% of the peak summer values, respectively. These results support the hypothesis that vitamin D and serum phosphorus concentrations vary significantly as a function of season.

These results have important implications for the management of Fall-born crias. Observations suggest that Fall-born crias are most susceptible to this syndrome. This

observation makes sense in that Fall-born crias never obtain any vitamin D reserves from summer sunshine. In contrast Spring-born crias store vitamin D during the summer and enter the winter with these reserves. Also Fall-born crias will be attempting to achieve their most rapid growth rate during the time of lowest vitamin D and phosphorus concentrations compared to Spring-born crias.

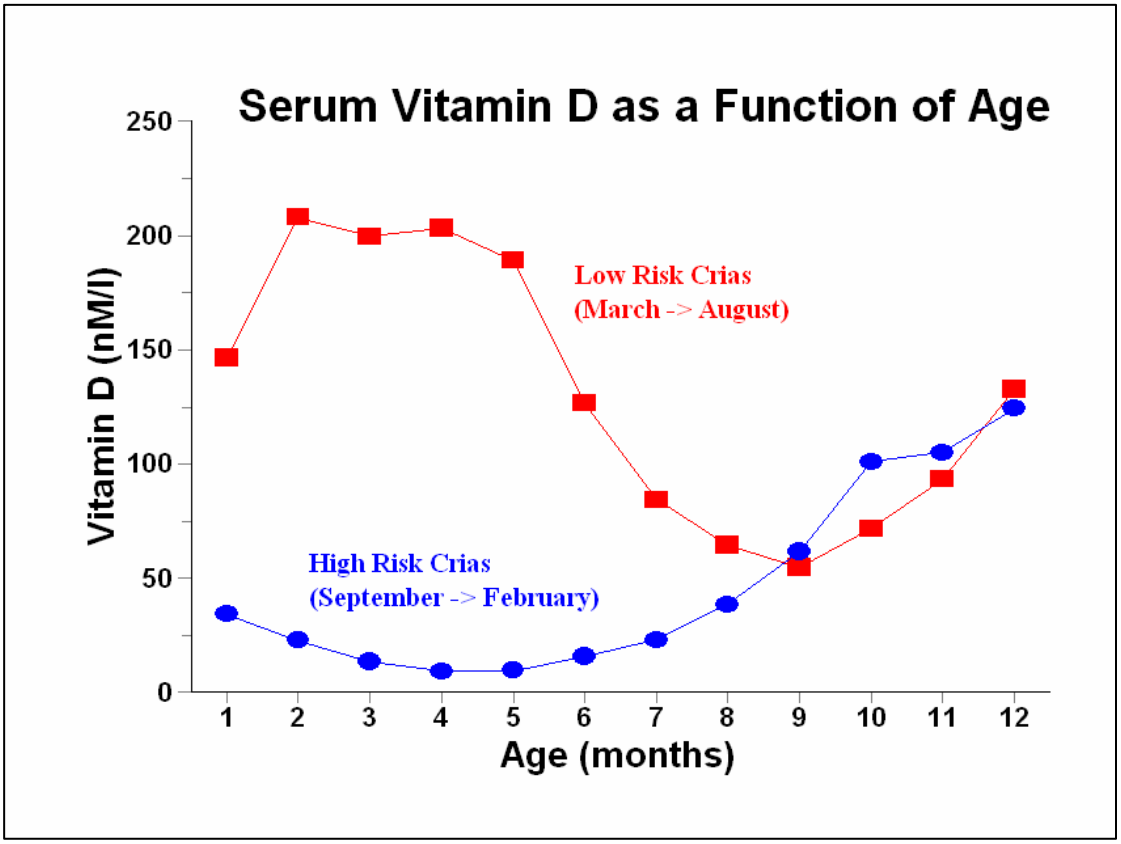

Figure 1. Comparison of serum 25-hydroxyvitamin D concentrations in crias over the first year of life categorized by month of birth.

Study Conclusions: Serum vitamin D and consequently serum P concentrations vary according to season with lowest values during the winter months. Fall-born crias will need to be carefully managed and vitamin D supplemented to prevent the rickets syndrome.

Reference: Smith, BB, Van Saun, RJ. Seasonal changes in serum calcium, phosphorus and vitamin D concentrations in llamas and alpacas. **American Journal Veterinary Research** 2001;62(8):1187-1193.

Study 3: Parenteral Supplementation

The objective of this project was to establish an appropriate level of injectable vitamin D supplementation to provide safe and therapeutically useful serum concentrations of vitamin D for the prevention of vitamin D deficiency disease in llamas and alpacas. Within this objective, we also wanted to determine if there would be any age differences in response to vitamin D supplementation. Thirty llamas and alpacas were assigned to 1 of 5 treatment groups based on level of vitamin D supplementation. All animals were given a single injection or oral bolus at the beginning of the study. Each treatment group was further subdivided by age (juvenile, teenage, adult).

Intramuscular injection of a commercial vitamin D preparation (product also contains vitamins A and E) increased serum vitamin D concentration above placebo injected controls for a period of 90-120 days from treatment. Based on our assessment of these data, we would recommend that a dosage between 1,500 to 2,000 IU vitamin D/kg body weight seems to maintain clinically appropriate serum concentrations to prevent deficiency disease. An interesting finding confirming other unpublished data shows a significant age effect on Ca and P concentrations in the llama. Serum phosphorus concentration declines over the first year of life from up over 9 mg/dl coming down to adult concentrations. Vitamin D concentrations were not influenced by age. Relative changes in serum vitamin D concentrations following a single oral or intramuscular administration of vitamin D at a rate of 4,000 IU/kg found a lower than anticipated oral bioavailability of vitamin D following a single treatment.

Study Conclusions: Intramuscular injection of commercial vitamin D preparations at a dosage between 1500-2000 IU/kg (700-900 IU vitamin D/lb) body weight can effectively increase serum vitamin D concentrations for 90 days. For a product containing 75000 IU/ml of Vitamin D, this is equivalent to 0.9 to 1.2 ml/100 lb body weight dosage. These injections can be used to treat a clinical animal or used to boost vitamin D status in an effort to prevent the problem. Preventive treatment should be given in the Fall.

Study 4: Vitamin D Toxicity

Unfortunately, vitamin D is one of the more toxic essential nutrients. Given the usual adage that if a little is good, a lot is better; we initiated a study to assess the degree of toxicity vitamin D has in the llama and alpaca. Initially 12 llamas and alpacas were assigned to 1 of 4 treatment groups with varying levels of a single vitamin D intramuscular injection. Serum vitamin D concentrations showed a dose-dependent response; however, no clinical evidence of acute vitamin D toxicity was appreciated. Following these results, a single animal was treated with a higher dosage (64,000 IU/kg BW) and again no acute toxicity was observed on clinical or postmortem evaluation. In reviewing these results, serum vitamin D and P concentrations were in the toxic range for most other species. The high serum P values are of concern since they may result in a precipitation of Ca and P crystals in blood, urine and body tissues over time. A third trial using 9 llamas at 3 vitamin D treatments was initiated using an emulsified form of vitamin D, as was used in the previous supplementation studies. Again dose-dependent vitamin D

responses were observed, but no clinical evidence of acute toxicity. Further data analyses are pending for this study, but preliminary impressions suggest that llamas and alpacas seem somewhat resistant to acute vitamin D toxicity. Long-term toxicity problems were not addressed in this study and need to be of concern given the observed changes in serum P concentrations.

Study Conclusions: Llamas and alpacas seemingly are seemingly tolerant of acute vitamin D toxicity. However evidence is present that higher doses of vitamin D may result in altered P metabolism with the possibility of Ca and P precipitation in urine and tissues. Vitamin D supplementation should be approached carefully and under the guidance of a veterinarian. **We do not recommend increasing the suggested treatment dosage of vitamin D as there is no evidence of improved effect and suggestions of deleterious effects to animal health are evident.**

Study 5: Oral Vitamin D Supplementation

The final study completed was an attempt to determine a reasonable level of dietary supplementation of vitamin D to maintain what would be considered appropriate serum concentrations of vitamin D. It was assumed that if we can maintain serum vitamin D concentrations at these defined levels, based on comparisons between clinical and non-clinical animals, we can prevent this rickets syndrome. A total of 32 llamas and alpacas were separated into 3 age groups (juvenile, teenager, adult) and assigned to 1 of 4 dietary treatment groups differing in amount of oral Vitamin D supplementation. After 7 weeks of the feeding trial it was apparent that these supplementation levels were not sufficient and the supplementation rates were increased 10x and fed for an additional 5 weeks. The original dosing scheme was set to 0.5x, 1x and 2x the NRC recommended dosages for sheep and calves. Increases in serum vitamin D concentrations were noticed within 1 week of feeding the higher levels in all treatment groups. Preliminary data would suggest adequate serum Vitamin D concentrations may be maintained with daily supplementation at 33 IU/kg body weight daily, but further data analyses are needed. Lower dosages of vitamin D did induce some changes in serum P concentrations, but did not influence vitamin D values. Preliminary data from this study supports our earlier findings that bioavailability of oral Vitamin D seems to be low in llamas and alpacas.

Study conclusions: Preliminary estimates suggest that llamas and alpacas require a daily supplementation of vitamin D at a rate of 33 IU/kg body weight (15 IU/lb body weight) to maintain sufficient serum concentrations of vitamin D to prevent rickets. This is much higher than observed for other species (6.6 IU/kg body weight), but are consistent with previous findings of lower vitamin D availability and support the clinical observation of greater vitamin D problems in llamas and alpacas compared to other species.

Summary and Conclusions

Results from this series of studies funded by Willamette Valley Llama Association and Mark Morris Foundation have allowed us to absolutely identify seasonally low vitamin D

concentrations as the inciting cause of hypophosphatemic rickets syndrome in growing llamas and alpacas. We have also determined treatment and prevention protocols based on appropriate supplementation of vitamin D. Owners are also cautioned to not be too aggressive with vitamin D supplementation, especially injected forms, as there is the potential for toxicity problems. We would hope that following our final analysis of the oral supplementation project, dietary recommendations can be given to feed companies to help determine appropriate levels of vitamin D incorporation in commercial products.