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MONITORING OF PHYSIOLOGICAL CHANGES OF URIC ACID CONCENTRATION IN THE BLOOD OF SNAKES

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ABSTRACT

The evaluation of uric acid concentrations in the blood of snakes is a crucial tool in the diagnosis of gout and renal disease; both prevalent diseases in captive reptiles. However, without an understanding of the physiological fluctuations in uric acid levels and the absence of distinction that makes pathological changes, biochemical parameters are devalued. This study focuses on investigating the relationship between feeding rate and plasma-uric acid concentrations of snakes. The aim of this investigation is to facilitate a better understanding of the feed-induced changes that occur, and to render the analysis of this biochemical parameter as a more potent diagnostic tool. A total of 10 snakes were used in the study and the basal concentration of uric acid was established prior to feeding via blood biochemical analysis. The snakes were then fed rats and successive postprandial blood samples were taken for the monitoring of uric acid levels. The results demonstrated that feeding led to substantial elevations in the uric acid values, whereby postprandial concentrations were significantly elevated for up to 5 days after feeding. The postprandial elevations in uric acid documented in these snakes were of similar levels reported in snakes afflicted with gout or renal disease. The results demonstrated the significant changes that occur to uric acid levels after feeding, and highlights the resemblance between postprandial increases in uric acid and concentrations reported in snakes suffering from renal disease or gout. To avoid a misdiagnosis and to distinguish transient postprandial hyperuricemia from pathological elevations, collecting sufficient anamnestic data on time since last feeding in performing repeated sampling after one week period of fasting is suggested.

Key words: feed-induced changes; uric acid; snakes

INTRODUCTION

The analysis of biochemistry is a powerful diagnostic tool and an essential part of any diagnostic work-up of patients in the veterinary field. However, unlike in small

animal medicine, there remain significant gaps in our understanding of physiological changes and variables affecting reptilian biochemistry resulting in the devaluation of biochemical analysis as a diagnostic tool at this time. With the exponential rise in the number of reptiles in the UK, it is becoming increasingly crucial that our understanding of these animals develop alongside their increase in numbers.

Metabolic diseases are among some of the most frequently presented conditions in reptiles in captivity. Between 1992 to 1996 McWilliams and Leeson [6] found a prevalence of 84.4 % of metabolic disease in lizard patients were attributed to husbandry malpractice and dietary indiscretions. With the increased awareness of reptile owners and progression in exotics medicine, this statistic may improve but metabolic diseases remains a current issue in reptilian medicine.

Certain species of reptile exhibit elevated uric acid levels during hibernation, thought to be due to the reduced renal tubular blood flow at low temperatures experienced during the hibernation period [8].

Gout may be classified as either primary or secondary. Primary gout is the result of an overproduction of uric acid related to an innate metabolic disorder. Secondary gout is attributed to chronic disease states that offset the normal balance between production and excretion of uric acid (e.g. chronic renal disease, starvation, hypertension, use of nephrotoxic pharmaceuticals, such as gentamycin) [9].

However, gout is a common affliction in reptilian patients, it is not a common problem in general veterinary medicine. Current diagnostics of gout in reptiles combines clinical presentation, assessment of the biochemical panel (namely uric acid), radiography and biopsies, with the latter being definitive. However, in the detection of gout, diagnostic imaging and biopsies are insensitive in the early stages of the disease, leaving the veterinarian only the clinical presentation and biochemical evaluation as diagnostic options [7].

Numerous factors have been reported to influence the biochemistry of reptiles, including the season, hormones and diet (depending on the time of the blood collection) [5]. Understanding variations in serum uric acid concentrations in healthy reptiles is essential for assessing hyperuricemia in patients potentially affected by gout. However, reference ranges for uric acid provided in the current literature are broad and do not account for such physiological fluctuations rendering such information less sensitive and potentially misleading conclusions [1].

With the ability to detect hyperuricemia prior to the extensive deposition of urate crystals in tissues would allow clinicians to identify risk patients and develop appropriate therapeutic strategies.

The aim of this study was to determine feed-induced changes to serum uric acid concentrations in 7 species of snake.

MATERIALS AND METHODS

For this study, ten adult snakes of various species were used: Burmese Python (*Python bivittatus*), Bulgarian Ratsnake (*Elaphe quatuorlineata*), Boa Constrictor (*Boa constrictor*), Carpet Python (*Morelia spilota*), Taiwanese Beauty Snake (*Orthriophis taeniurus freiesi*), Common Kingsnake (*Lampropeltis getula*) and Rainbow Boa (*Epicrates cenchria*).

The snakes were housed individually in terrariums with glass front panels and with the slots in the side panels for ventilation. Each snake was kept in temperature controlled conditions at approximately 25 °C (± 5 °C). Prior to pre-prandial sampling, each snake underwent a minimum fasting period of 14 days to avoid anomalies from previous meals. The snakes were fed rats (*Rattus norvegicus*) and mice (*Mus musculus*) and the body weight was recorded with each meal. Water was given *ad libitum*.

Blood samples were collected and run prior to feeding to establish baseline concentrations of uric acid in each snake. Uric acid concentrations were measured subsequent to feeding and daily thereafter until serum concentrations returned to near basal levels.

The blood was collected via the ventral coccygeal vein with a 23-gauge needle and the samples were collected into heparinized blood collection tubes. If blood collection from the ventral coccygeal vein was not possible, it was obtained via cardiocentesis. The samples were then centrifuged and a volume of 5 µl of serum was obtained with a micropipette and was aliquoted for analysis. For the measurement of uric acid concentrations from the serum, immunoassays were performed with the LifeAssays Canine CRP test kit (Life Assays AB, IDEON Science Park, Sweden), evaluating each sample, the level of CRP in $mg.l^{-1}$.

The one-way analysis of variance (ANOVA) was performed to determine any statistically significant differences

between the means of pre-prandial and post-prandial serum uric acid concentrations; the significance was assumed when $P < 0.05$.

RESULTS

The mean pre-feeding and post-feeding serum uric acid concentrations in the blood of snakes are shown in Table 1. and Fig. 1.

Table 1. Mean pre-feeding and post-feeding serum uric acid concentrations in blood of snakes

Days post feeding	Mean serum uric acid [mg.l^{-1}]
0	253.01
1	784.65
2	1251.88
3	988.56
4	642.80
5	414.33
6	403.52
7	363.13
8	326.34
9	299.08

Table 2. Pre-feeding against post-feeding uric acid concentration results from one-way ANOVA, with significance assumed at P < 0.05

Days post feeding	P-value
1	0.00015
2	0.00013
3	0.00003
4	0.00001
5	0.01729
6	0.07928
77	0.12153
8	0.25678
9	0.45148

The post-prandial levels of uric acid rose substantially in all snakes with a mean peak concentration reaching 1251.88 mg.l^{-1} (Table 1). Serum uric acid reached peak concentrations between 1 and 2 days in the blood of all snakes, with maximum recorded levels reaching 2524.3 mg.l^{-1} in Morelia spilota and minimum 578.4 mg.l^{-1} in Python bivittatus. The majority of the snakes studied showed similar patterns of sharp elevations in uric acid, followed by a more gradual decline and returning to basal concentrations approximately nine days after feeding.

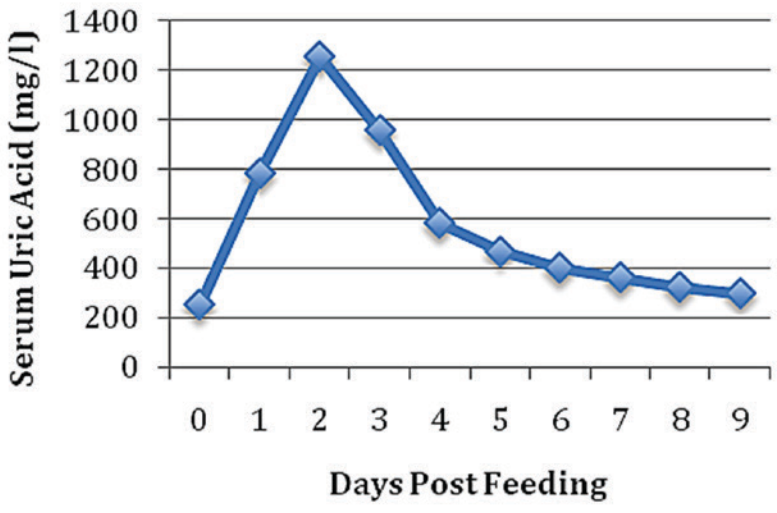

Fig. 1. Changes in mean pre-feeding and post-feeding serum uric acid concentrations in snakes

Results from the one-way ANOVA demonstrated pre-prandial and post-prandial uric acid profiles to be statistically significant ($P < 0.05$) up until the fifth day after feeding. From days 1—4 uric acid values were substantially elevated; $P < 0.001$, indicating marked deviations from the basal concentrations. From day 5, we observed a reduction in the mean uric acid concentration (414.33 $mg.l^{-1}$) with a significance value of $P < 0.05$. From day 6 onwards, there was a steady reduction in the mean concentration and we found no significance in these samples ($P > 0.05$).

DISCUSSION

This study has visibly demonstrated that significant post-prandial increases of serum uric acid concentration occur in snakes. Maixner et al. [4] demonstrated the effect of feeding on uric acid concentrations in other species of captive reptile: savannah monitor lizards (*Varanus exanthematicus*), black rat snakes (*Elaphe obsoleta*) and the Gila monster (*Heloderma suspectum*). Post-prandial serum uric acid levels found in this study revealed levels of hyperuricemia similar to those documented in reptiles suffering from renal disease or gout. Reptiles presented with gout show uric acid levels over 2-fold higher than the recorded baseline levels [2], analogous with post-prandial concentrations documented in this study. Although it is difficult to find a definitive measure of hyperuricemia due to differing physiologies among snake species, some reports define hyperuricemia as serum uric acid concentration greater than 150 $mg.l^{-1}$ [3]. Post-prandial values recorded in our present study were substantially higher than levels with peak concentrations reaching 5 times higher than recorded pre-prandial levels. These results provide compelling evidence that feeding has a quite marked effect on uric acid measurements to the extent at which the reptilian clinician may misinterpret these results as an indication of disease.

An investigation into the effect of temperature on the metabolic rate in the Bolivian Silverback (*Boa constrictor amarali*) found that the ambient temperature had a profound effect on the duration of digestion and also digestive efficiency [10]. With this, we can assume that under conditions with more variable temperatures, in particular lower temperatures (not uncommon in captive reptile husbandry), we may see changes in the relationship between feeding and uric acid concentrations.

For the exotics veterinarian this has quite significant implications on the way biochemistry panels are evaluated. It highlights the importance of collecting sufficient anamnestic data prior to carrying out further diagnostic measures. As highlighted, post-prandial effects on serum uric acid concentrations may last up to 5 days or more. It is therefore rational to suggest that information on the time interval since last feeding should be included in the anamnesis. Clinicians should also note that reptiles presented with hyperuricemia should be sampled and re-assessed no sooner than one week of fasting to allow for more accurate interpretation of uric acid concentrations and to avoid misdiagnosis.

CONCLUSIONS

To conclude, this study highlights the importance of feed-induced changes in serum uric acid concentrations in the blood of snakes. It is evident that post-prandial changes in uric acid may mimic degrees of hyperuricemia as those seen in reptiles suffering from gout or renal disease. We also discovered that with the exclusion of such information in the anamnesis, there is room for error and misinterpretation in the diagnostic work-up. The clinical relevance of these results are found while determining the time interval required for re-sampling for a more accurate representation of true basal levels of uric acid in a patient and shown to be approximately 1 week after feeding. This study also highlights the difficulties encountered when providing generalized reference values for biochemical parameters in reptiles. With substantial differences among snake species and broad reference values, there lay a risk of misinterpretation and potential misdiagnosis if it is not possible to control major variables (i.e. feeding). With the further development of reptilian medicine, we would hope to find more species specific databases, allowing for more accurate reference values available for the clinician, rendering the analysis of biochemistry a more powerful diagnostic tool.

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