

## 12. Use of Exogenous Creatinine to Evaluate Kidney Function in Hydration and Dehydration Conditions of Camels

A. Kamili\*, M. Bengoumi, M. Oukessou, B. Faye and H. Lefebvre

*Corresponding author email: asma\_kamili@yahoo.fr*

### Introduction

The dromedary camel is an animal well adapted to extreme temperature conditions and osmotic fluctuations (Yagil, 1986). Camel adaptation to dehydration is the consequence of its anatomic and physiologic particularities (Bengoumi *et* Faye, 2002). It has been shown, that dromedary camel kidney function is one of the most important factors of its ability to adapt to extreme conditions of osmotic stress and additional water needs as during milking periods (Yagil, 1993, Bengoumi *et al.*, 1993).

### Objectives

This trial aims to study kidney function in camel dromedary under normal hydration and dehydration conditions *via* follow up of glomerular filtration using exogenous creatinine as marker.

### Materials and Methods

This trial was carried out at the Hassan II Agronomic and Veterinary Institute (IAV Hassan II in Rabat-Morocco) on six 7-10 year old females; animals were fed before and during this experiment with concentrated feed (MARAA) at 2kg/animal/day which contains very little water. In addition, they received one bale of wheat straw (18kg) once per day in the morning and water was given *ad libitum* during normal hydration period. Body weights were assessed on experiment day using barymetric measurements (Schwartz *et al.*, 1992).

### Experimental Protocol

#### *1<sup>st</sup> Phase:*

##### *Product and doses used*

To prepare the solution to be injected to dromedaries at 8g/100ml (8%), 40g creatinine (anhydrous powder) was progressively dissolved in 500 ml of distilled water, and sterilized by filtration using 0.22  $\mu$ m paper filter. The prepared solution was injected to animals at 16 mg/kg of body weight corresponding to 20 ml of the solution/kg of body weight. Volume injected to each animal was calculated on the basis of body weight assessed on the same day.

##### *Bloodsampling and plasma processing*

Blood samplings (8-10 ml) were performed on right jugular vein in a vacuum tube with anticoagulant at times T<sub>0</sub> (just before injection), 2 ; 6 ; 10 ; 20 ; 40 ; 60 and 90 min and 2 ; 4 ; 6 ; 8 ; 12 ; 18 and 24 h after injection. T<sub>0</sub> blood sampling was performed to determine basal blood creatinine. Blood samples were centrifuged for 30-45 min (3000g/min during 15 min) and plasma was stored at -20°C until creatinine dosage. Hematocrit, density and total proteins were performed on whole blood. To establish RCN, Neubauer cells counter was used

#### *Phase 2: Dehydration during 34 days*

Dehydration began the next day after completion of blood samplings which was spread over 24 hours. Camels were deprived from water intake and kept in stable where night and diurnal temperature conditions are under control (20°C-23°C). For animal welfare, camels dromedaries were examined every day to take body temperature and to observe their reactivity state to avoid possibly apathy and pain. Blood samplings were carried out at the beginning of this stage and every week to determine total proteins, hematocrit, density, Red Cells Number (RCN) and Mean Cell Volume (MCV) which were used as indicators of the camels dehydration status. At 34<sup>th</sup> day post water deprivation, dromedaries were subject to the same experimental protocol previously described, during hydration period, to follow up creatinine kinetics during a period of 24 hours.

### Creatinine determination

Plasma creatinine was analyzed using the Jaffe method.

## Data analysis

All parameters measured on the 6 dromedaries were used for data base conception in Excel and analyzed then as follows:

Comparisons of studied parameters means, in hydration and dehydration states were realized by Excel software, using matched means comparison function with  $p=0.05$  to consider the test significant. Results are expressed as mean $\pm$ standard error.

Pharmacokinetic analyses were performed by WinNonlin Software (Version 5.2, Build 200701231637 Core version 18 Sept 2006) using non compartmental approach.

## Results and Discussion

To compare parameters studied on camels, corresponding to normal hydration and dehydration periods (34 days of thermic and hydric stress), paired means comparison tests were used. Equality esperances test for paired observations in Excel offers the possibility to compare means with Student test;  $p=0.05$  was retained as meaning threshold test. Pharmacokinetic data analysis were performed using non compartmental approach, considered to be more suitable especially when sampling period is 24 hours, because it doesn't need specific mathematic modeling. Laroute *et al.*, (1999) reported also that lonely parameter required is AUC which is then easy to calculate and extrapolated party of AUC should not exceed 15% of total AUC. In the present study, at the moment of GFR calculation in normally hydrated and dehydrated states, extrapolated party of curve has as mean respectively  $9.3 \pm 6.3\%$  and  $11.2 \pm 4.9\%$ .

Camels dromedaries of the present study showed a body weight decrease of 15% following 34 days dehydration, which can be interpreted as adaptation to lack of water. These results are different from Bengoumi (1993) who reported that 14 days water deprivation caused body weight decrease of 35%. This difference can be linked to ambient temperature ( $45^{\circ}\text{C}$ ) and dehydration severity. According to Djegham and Belhadj (1986), camel dromedary resistance to water deprivation is due to its ability to mobilise its water storage and to transfer it from one to another compartment. Thus, camel dromedary is able to lose up to 25% of its total body water without any dehydration symptoms. Hematocrit mean values in the six dromedaries ( $27\pm 1\%$  in normal hydration state and  $28\pm 2\%$  in dehydration state) are included in the interval of usual hematocrit mean values [20-33%] as described by Yagil *et al.* (1974) and are lower than those reported by Bengoumi (1993) with values of 30% in hydration state and 38% in dehydration state, but still compared to those of Yagil *et al.* (1974) with  $28.5\pm 0.82\%$  in summer and  $32\pm 1.02\%$  in winter. Differences between these values can be explained by season and hydration status which affect directly this parameter. So then, it's important to know conditions of normal values in dromedary camel (Yagil *et al.*, 1974). Hematocrit mean values in dromedary camels in normal hydration and dehydration states did not show any significant difference. This can be explained by individual variations that should mask this effect or because dehydration state was not so severe to influence this parameter. Thus, this parameter can be considered as later parameter to detect hydration state in the dromedary camel. RCN in this trial ( $8.6\pm 1.4\times 10^6/\text{mm}^3$ ) is included in physiologic values interval as reported by Yagil *et al.*, (1974) ( $3.8\times 10^6/\text{mm}^3$  and  $12.6\times 10^6/\text{mm}^3$ ). Dehydration caused a significant decrease in RCN which is in agreement with data reported by Yagil *et al.*, (1974) as hematocrit and RCN follow same evolution. MCV was influenced by dehydration. It has been significantly increased (from  $31.9\pm 4.6\times 10^{-7}\text{ mm}^3$  to  $48.2\pm 7.3\times 10^{-7}\text{ mm}^3$ ) after 34 days of water deprivation. Results of this study showed significant plasma creatinine increase with rate of 30% with dehydration, except for camel A (from  $1.18\pm 0.28\text{ mg/dl}$  ( $104\pm 25\text{ }\mu\text{mol/l}$ ) to  $1.53\pm 0.14\text{ mg/dl}$  ( $135\pm 12\text{ }\mu\text{mol/l}$ )). These results agree with Bengoumi's work (1993). Plasma creatinine values in dromedaries seem to be higher than those reported in other species (Soliman et Shaker, 1967). In our study, 34 days of water deprivation in camels induced significant GFR diminution (from  $1.33\pm 0.22\text{ ml/min/Kg}$  to  $1.06\pm 0.21\text{ ml/min/kg}$ ) which presents a decrease of 20%. These results are in agreement with those of Bengoumi (1993) who found GFR decrease of 60% after 13 days of water deprivation and then it increased after rehydration. Explanation of these phenomena can be attributed to hormonal factors.

## Conclusions and Recommendations

Significant decrease of body weight in camel dromedary in dehydration conditions is an adaptation way to water restriction and RCN and MCV can be used as dehydration state indicators. The role of the kidney to minimize water loss is the result of both anatomic and hormonal factors

controlling glomerular filtration. Indeed, GFR is lower than that reported in other animal species and has significantly decreased under effect of dehydration. These results should be taken into account during drugs administration. In this effect, this animal should be considered as a model for studies of dehydration effect on hormones and enzymes implicated in water metabolism regulation.

Use of exogenous creatinine in *bolus* for kidney function evaluation in camel dromedary is a practical method, reliable, quick, not expensive and has less risks for animals compared to other methods based on urine collection. Nevertheless, other investigations are necessary in large number of animals to study creatinine tubular secretion, particularly in dehydration conditions and according to the sex. Fifteen blood samplings during 24 hours is a tedious work in routine practice. So then, it's very interesting to draw up limited strategy for blood samplings in order to determinate blood samplings number and best time with minima risks errors.

## References

- Alamer M., 2006. Physiological responses of Saudia Arabia indigenous goats to water deprivation. *Small Ruminant Research*. 63: 100-109.
- Bengoumi M., 1993. Biochimie clinique du dromadaire et mécanismes de son adaptation à la déshydratation. *Thèse de doctorat Es-Sciences Agronomiques*. Institut Agronomique et Vétérinaire Hassan II-Rabat.
- Bengoumi M., Riad F., Giry J., De La Farge F., Safwate A., Davicco M.J and Barlet J.P, 1993. Hormonal Control of Water and Sodium in Plasma and Urine of Camels during Dehydration and Rehydration. *General and Comparative endocrinology*. 89: 378-386.
- Bengoumi M. and Faye B., 2002. Adaptation du dromadaire à la déshydratation. *Sécheresse*. 13 (2) 121-129.
- Djegham M. and Belhadj O., 1986. Comportement de thermorégulation et résistance à la privation d'eau chez le dromadaire, Variations saisonnières des profils biochimique et hématologique chez le dromadaire. *Maghreb Vétérinaire*. 2(10).
- Kamili A., Bengoumi M. and Faye B., 2006. Assessment of body condition and body composition in camel by barymetric measurements. *Journal of Camel Practice and Research*. 13 (1): 67-72.
- Kumar R., Singh A.P. and Rai A.K., 1999. Pharmacokinetics, bioavailability and dosage regimen of sulfadimidine in camels (*Camelus dromedarius*) under hot, arid environmental conditions. *Vet. Res*. 30: 39-47. inra/Elsevier, Paris.
- Laroute V., Lefebvre H.P, Costes G. and Toutain P.L., 1999. Measurement of glomerular filtration rate and effective renal plasma flow in the conscious beagle dog by single intravenous bolus of iohexol and p-aminohippuric acid. *J. Pharmacol. Toxicol*. 41 : 17-25.
- Shwartz H.J and Dioli M., 1992. The one humped camel in eastern Africa. A pictorial guide to diseases health care and management. Weikersheim, Verlag Joseph Nargmf ; 282 p.
- Soliman M.K and Shaker M., 1967. Cytological and biochemical studies on the blood of adult camels. *The Indian. Vet. J*. 44(12): 989-995.
- Yagil R., Sod-Moriah U.A. and Meyerstein N., 1974. Dehydration and Camel blood. II. Shape, size and concentration of red blood cells. *Am.J. Physiol*. 226 (2): 301-304.
- Yagil R., 1993. Renal function and water metabolism in the dromedary. *Moving Points in Nephrology Contrib. Nephrol. Basel, Karger*. 102 :161-170.