THE EFFECTS OF DIFFERENT ANAESTHETIC REGIMES USING PROPOFOL AND DIFFERENT SEDATIVES ON THE CONCENTRATION OF PLASMA CORTISOL AND GLUCOSE IN CAMELS (Camelus dromedarius)

G.A. Mohamed¹, A.A. Sanhouri¹, R.O. Ramadan² and A.A. Almubarak²

¹Division of Animal Medicine and Surgery, College of Veterinary Medicine, Sudan University of Science and Technology, Khartoum, Sudan and ²Department of Clinical Studies, College of Veterinary Medicine and Animal Resources, King Faisal University, Alhasa, Saudi Arabia

ABSTRACT

Eight male camels were subjected to clinical examination to ensure their healthy status and parasitic free. Normal sampling day started at 8:30 a.m. and lasted at 3:30 p.m. and it served as control day. Another day the animals were fasted for 24 hours to resemble the fasting during anaesthesia. Propofol @ 2 mg kg⁻¹ injected via an indwelling intravenous catheter. Sampling procedures include pre-injection, served as base line values, during anaesthesia more frequent sampling were carried out, followed by the recovery time. The same sampling protocols followed for the other anaesthetic regimes (propofol 2 mg kg⁻¹\xylazine 0.25 mg kg⁻¹ and propofol 2 mg kg⁻¹\xylazine 0.25 mg kg⁻¹\diazepam 0.25 mg kg⁻¹).

A significant variation was observed in both cortisol and glucose values (P<0.01) of these anaesthetic regimes, on the other hand the recovery time from anaesthesia showed the highest Cortisol and glucose values compared with the base line values (pre-injection) and the anaesthesia time.

Key words: Camel, cortisol, diazepam, glucose, propofol, xylazine

Studies conducted in early decades to develop new and safe injectable intravenous anaesthetic demonstrated that some derivatives of phenol had hypnotic properties; this resulted in the development of a new molecule 2, 6.di-isopropyl phenol. The efficiency of propofol anaesthesia with xylazine and diazepam premedication in camels was studied by Fahmy *et al* (1995) and Al-Mubarak (2008)

The aim of the present study was to estimate the concentration of cortisol and glucose in peripheral circulation during anaesthesia, after recovery period from anaesthesia and at the two hour after recovery using different anaesthetic regimes

Materials and Methods

Animals

Clinically sound male dromedary camels (n=8) with mean age 6.2±1.3 years and body weight 353 ±38.5 kg. They were housed in open sheds at experimental farm of the College of Veterinary Medicine. All camels were subjected to clinical examination to ensure their healthy status and were made parasite free, camels were fed roughages concentrate mixture (molasses) and allowed free access to water, camels were fastened 24 hours prior to anaesthesia injection.

Experimental procedures

The experiment was carried out between 8:30 in the morning and lasted at 3:30 p.m. in each experiment anaesthesia injected and blood samplings were obtained via jugular catheter fixed on the day prior to the start of the experiment.

Anaesthetic regimes were:

Regime (1): propofol @ 2 mg kg⁻¹

Regime (2): xylazine @ 0.25 mg kg⁻¹ + propofol @ 2 mg kg⁻¹

Regime (3): xylazine @ 0.25 mg kg⁻¹ + diazepam @ 0.25 mg kg⁻¹ + @ propofol 2 mg kg⁻¹

SEND REPRINT REQUEST TO R.O. RAMADAN email: rramadan@kfu.edu.sa

Sampling

4 ml blood were collected in heparinised vials, centrifuged at 5000g for 10 minutes and plasma decanted within 25 minutes after collection and immediately stored at -20°C until cortisol concentration assay.

A 2.5 ml of blood were collected in fluoride oxalate vials, centrifuged and plasma glucose concentration was analysed within 24 hours.

In each anaesthetic regime two samples were collected as preinjection samples (served as base line values), during anaesthesia and on the recovery time (immediately when animals moved their head and when animal get up and walked) and two hours after recovery one sample was drawn.

Seven samples were taken in each anaesthetic regime.

Laboratory procedures

Plasma cortisol concentration was estimated by radio-immunoassay (RIA), while plasma glucose concentration was estimated using glucose kit (Biosystem S.A. Costa Brava 30, Barcelona, Spain).

Statistical analysis

Statistical comparisons were made using a one-way ANOVA and data were presented as mean±standard deviation (S.D).

Results

Table 1 showed that plasma cortisol concentration at recovery time was significantly

higher (P<0.01) as compared with the base line values (pre-injections values), during the anaesthesia and at the two hours after recovery from anaesthesia in all mentioned anaesthetic regimes.

The plasma glucose concentrations (Table 2) of camels during the recovery time was significantly higher (P<0.01) than that of the per-injection, duration time of anaesthesia and at the two hours following recovery from anaesthesia in all different anaesthetic regimes.

The time of anaesthesia duration in the anaesthetic regimes (propofol alone, propofol and xylazine, and propofol, xylazine and diazepam) were calculated as mean±SD, 13±2.4, 35.6±10.8, and 35.2±3.6, respectively.

The anaesthesia duration time was considered as the period during which the animal showed signs of unconsciousness, absence fo reflexes, and responsed negatively to pain stimuli.

Total recovery presented as mean \pm SD, 22.8 \pm 6.3, 69.4 \pm 13.6 and 95 \pm 15.8 in propofol alone, propofol and xylazine, and propofol, xylazine and diazepam anaesthetic regimes, respectively. Total recovery time was considered as the total time calculated from the time of induction of anaesthesia until recovery was attained.

Discussion

During this study efforts were made to throw some light on the concentrations of the plasma

Table 1. Mean ±SD of plasma cortisol concentrations (ng\ml) during the anaesthesia time in different anaesthetic regimes in dromedary camel (n=8, male).

Anaesthesia time Protocols	Pre injection	During anaesthesia	Recovery	2 hours
Propofol	14.50±3.87 ^c	14.14±3.31 ^a	37.03±4.90 ^a	24.19±9.78 ^a
Propofol + Xylazine	15.01±3.61 ^b	9.95±6.43 ^b	29.24±3.92 ^b	17.66±2.75a ^b
Propofol + Xylazine +Diazepam	13.78±3.50 ^b	9.17±6.11 ^b	24.88 ± 4.17^{b}	16.41 ± 4.00^{b}
Significant	N.S	**	**	*

Table 2. Mean ±SD of plasma glucose concentrations (mg\dl) during the anaesthesia time in different anaesthetic regimes in
dromedary camel (n=8, male).

Anaesthesia time Protocols	Pre injection	During anaesthesia	Recovery	2 hours
Propofol	119.60±37.08	124.20±35.07 ^a	178.18±14.41 ^a	143.57±23.18
Propofol + Xylazine	121.53±23.05	105.35±35.15 ^b	151.44±10.08 ^b	127.46±7.18
Propofol + Xylazine +Diazepam	113.71±24.68	97.04±39.05b ^b	137.71±16.07 ^b	129.97±28.57
Significant	N.S	**	**	*

N=8

Sig.: significant *: significant at P < 0.05

 cortisol and glucose using propofol (@ 2 mg kg⁻¹) as intravenous anaesthetic agent either alone or with premedication. However, the mechanism by which propofol reacted on cortisol concentrations was not fully elucidated especially in camelids.

Stress is known to compromise animals welfare through different bioactive pathway such as clinical, physiological, behavioural and other changes (Kannan *et al*, 2000; Ali *et al*, 2001). Stress may have negative consequences on the reproductive potential of animals (Dobson *et al*, 2001; Sevi *et al*, 2001a,b).

Propofol as intravenous hypnotic agent in anaesthetic dose blocked the rise in plasma cortisol concentration when compared to pre-injection values during sleeping time, which is in agreement with the work on goats using pentobarbitone and etomidate (Sanhouri et al, 1991; Silver and Taylor, 1988) in goats and ponies consecutively. The decrease in plasma cortisol concentrations from peak values vary according to the type and duration of stressor in goat. The increase in the plasma cortisol and glucose concentrations in all anaesthetic regimes under study was evident during recovery time and that was associated with struggling which took place as animals become aware of their surrounding and attempt to stand or having an increase in stressor such PCo₂ value (Sanhouri et al, 1991). However, the increase was not comparable to a high intensity stressor such as that seen during transportation. This response during recovery indicated that total depression at any part of the hypothalamus-pituitary adrenocortical axis did not take place and the HPA was still responsive and this prevented animal from anaesthetic emergency (Kehlet, 1984). The values of the plasma cortisol and glucose concentrations after two hours of recovery started to decline and this is in agreement with the decline of cortisol concentrations reported after three hours of recovery from propofol infusion in man (Kay et al, 1985)

Propofol when administrated with xylazine or- and with diazepam produced lower increase in plasma cortisol concentrations during the recovery time as compared with anaesthesia with propofol alone, which indicated that propofol is a safe anaesthetic agent with moderately smooth recovery. Similar results were reported by Ali *et al* (2001) for using xylazine in camels during transportation stress. The plasma glucose concentrations during the recovery time using propofol/ xylazine anaesthesia is mimicking the effect of this protocol on cortisol suggesting a synergistic effect of cortisol on glucose concentration (Eigler *et al*, 1979). The regime of propofol/ xylazine/ diazepam on plasma cortisol concentrations during the recovery time showed a remarkable decrease this seems to be in accordance with Jones *et al* (1976) who reported a GABAergic control on HPA activity. On the other hands our results are in accordance to the work of Morishima *et al* (1980) in ruminants. The results were also in agreement with that detomidine-HCl (alfa-2 adrenoceptor agent) caused decreases in pituitary-adrenocortical activity or inhibition of steriogenesis (Luna *et al*, 1996).

The decrease on plasma glucose concentration during the recovery from anaesthesia with propofol, xylazine and diazepam compared with the other anaesthetic regimes also reflect the effect of the diazepam on the plasma glucose concentrations and the reduction of the increase in the plasma glucose concentrations were in agreement with the suppression of the stress response to transportation by diazepam in goats (Dundee, 1989). Other benzodiazepine, midazolam, has been shown to reduce the catecholamine response to electrical stress in rats (Prada *et al*, 1980) and surgery stress in dogs (Glisson *et al*, 1983).

The decrease on the plasma glucose concentrations during anaesthesia with propofol xylazine and / or diazepam compared with anaesthesia using propofol alone was in agreement with that plasma glucose concentration is decreased after administration of xylazine (Custer *et al*, 1977).

In conclusion, the stress response reflected in this series of experiments by changes in the HPA axis and the sympathoadrenal system, is under the control of (nor) adrenergic and GABAergic pathway centrally or possibly peripherally. *In vitro* studies which hopefully would avoid side-effects may provide more information concerning control of HPA activity.

References

- AI Al-Mubarak (2008). Experimental evaluation of propofol total intravenous anaesthesia (TIVA) in dromedary camels. Journal of Camel Practice and Research 15(2):205-207).
- Ali BH, AL-Qarawi AA, Mousa HM and Mohammed SM (2001). Tyrosine ameliorates some of the clinical, biochemical and haematological effects of acute stress associated with transportation of dessert sheep. Veterinary Research Communications 25(6):503-510.
- Custer R, Krammer L, Kennedy S, Bush M (1977). Haematologic effects of xylazine when used for restraint of Bactrian camels. Journal of the American Veterinary Medical Association 171:899-901.

- Dobson H, Tabble JE, Smith RF and Ward WR (2001). Is stress really all that important?? Theriogenology 55(1):65-73.
- Dundee JW (1989). Pharmacology of intravenous anaesthetics and hypnotics. General Anaesthesia, 5th Ed. (ed) J.
 F. Nunn, J. E. Utting & B. R. Brown. pp 115-134, Butterworths London.
- Eigler N, Sacca L and Sherwin RS (1979). Synergistic interaction of physiologic increasment of glucagon, epinephrine and Cortisol in the dog. The Journal of Clinical Investigation 63:114-1123.
- Fahmy LS, Farag KA, Mostafa MB and Hegazy A (1995). Propofol anaesthesia with xylazine and diazepam premedication in camels. Journal of Camel Practice and Research 2:111-114.
- Glisson SN, Haddad W, Kubak MA and Hieber MF (1983). Midazolam action on catecholamine, cortisol and rennin responses to surgical stress in dogs. Anesthesiology 59A:239.
- Jones MT, Hillhouse EW and Burden J (1976). Effect of various, putative neurotransmitters on the secretion of corticotrophin- releasing hormone from the rat hypothalamus in vitro-A model of the neurotransmitters involved. Journal of Endocrinology 69:1-10
- Kannan G, Terril TH, Kouakou B, Gazal OS, Gelaye S, Amoah EA and Samake S (2000). Transportation of goat: effects on physiological stress responses and live weight loss. Journal of Animal Science 78(6):1450-1457.
- Kay NH, Uppington J, Sear JW and Allen Mc (1985). Use of an emulsion of ICI 35868 (propofol) for the induction and maintenance of anaesthesia. British Journal of Anaesthesia 57:736-742.

- Kehlet H (1984). The stress response to anaesthesia and surgery: release mechanisms and modifying factors. Clinics in Anesthesiology 2:315-339
- Luna SP, Taylor PM and Wheeler MJ (1996). Cardiorespiratory, endocrine and metabolic changes in ponies undergoing intravenous or inhalation anaesthesia. Journal of Veterinary Pharmacology and Therapeutics 19:251-258.
- Morshima HO, Aakuma K, Bruce Sl, Pedersen H, Dyrenfurth I, Daniel SS and Finster M (1980). The effects of diazepam on maternal and foetal stress responses in the sheep. Developmental Pharmacology & Therapeutics 1:364-371.
- Prada M, Pieri l and Picotti GB (1980). In: Catecholamine and Stress. Eds. Osain, Kjertiansky& Kopin, Korth Holland, Elsevier. pp 231-236.
- Sanhouri AA, Jones RS and Dobson H (1991). Pentobarbitone inhibits the stress response to transport in male goat. British Veterinary Journal 146:36-42.
- Sevi A, Annicchiarico G, Albenzio M, Taibi L, Muscio A and Dell'Aquila S (2001b). Effects of solar radiation and feeding time on behavior, immune response and production of lactating ewes under high ambient temperature. Journal of Dairy Science 84(3):629-40.
- Sevi A, Taibi L, Albenzio M, Muscio A, Dell'Aquila S and Napolitano F (2001a). Behavioral, adrenal, immune, and productive responses of lactating ewes to regrouping and relocation. Journal of Animal Science 79(6):1457-1465.
- Silver M and Taylor PM (1988). Adrenocortical responses to anaesthesia in sheep. Journal of Physiology 407:108.