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Short communication

Levels of glutathione peroxidase, lipoperoxidase and some biochemical and haematological parameters in gazelles anaesthetised with a tiletamin–zolazepam–xylazine combination

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Free radicals impair the biological functions of some proteins, enzymes, vitamins, and membrane lipids (Zintzen, 1972; McDowell, 1989). This leads to oxidation–reduction reactions in a variety of cells of different tissues including the nervous system, kidney, and liver. The effect on cell metabolism causes severe tissue damage, which, in turn, may lead to further pathological changes (Neri et al., 1993). However, anti-oxidants, formed by the cells, help to counterbalance such reactions and therefore play a vital role in the protection of the cells (Thomas, 1995).

The degeneration of tissues and blood cells that occurs occasionally after anaesthesia is believed to be due to anti-oxidant metabolism. The pro-oxidation effects of some general anaesthetics have been discussed (Khinev and Dafinova, 1993) and a variety of anaesthetics possessing different physico-chemical properties has been reported by these authors to affect the lipid peroxidation process, directly or indirectly, leading to the formation of malondialdehyde (MDA) in the body and tissue damage. The extent of the damage can be assessed by measuring the activities of serum enzymes and metabolites released from the cells.

The non-narcotic non-barbiturate injectable anaesthetic tiletamin–zolazepam (a 1:1 mixture of the dissociative anaesthetic tiletamine-HCl and zolazepam-HCl) is widely used in veterinary species (Silverman et al., 1983; Schobert, 1987; Payton and Pick, 1989; Ko et al., 1993). Its use in primates was reported to cause respiratory depression, peaking 10 min after administration (Booker et al., 1982). Intravenous (i.v.) administration in dogs has been shown to cause respiratory problems such as apnoea (Donaldson et al., 1989). Xylazine-HCl is an α_2-adrenergic agonist sedative with analgesic properties that has a significant depression effect on heart rate and respiratory system (DeRossi et al., 2003).

Although there have been many studies on the effects of different anaesthetics on antioxidants, lipid peroxidation, and biochemical and haematological changes in different species, to our knowledge there has been no work reporting the effect of tiletamin–zolazepam–xylazine in combination on the erythrocyte glutathione-peroxidase (GSH-Px) activity and lipid peroxidation in gazelles. In the present study, we aimed to investigate the effect of tiletamin–zolazepam–xylazine on the activity of erythrocyte GSH-Px, on serum MDA and several biochemical and haematological parameters before, during, and after the anaesthesia of gazelles.

We used 16 gazelles (*Gazella subgutturosa*), age range 1–4 years (mean 2.9 ± 0.3 years), held in the Wild Life Reservation Unit of the State Production Farm, Ceylanpmar, Sanliurfa, Turkey. All animals were apparently healthy with no clinical signs of disease. The animals were manually restrained and no sedatives or anaesthetics were used. Gazelles were starved overnight

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in cages prior to the investigation and handled according to the Ethical Board guidelines of Harran University. Each gazelle was anaesthetised with 10 mg/kg tiletamin–zolazepam (Zoletil 50, Virbac) and 1 mg/kg xylazine-HCl (Rompun, Bayer) intramuscularly (i.m.). Anaesthesia was produced within 3 min (average 2–8 min) and lasted about 1.5 h (mean 94.11 ± 26.23 min). Jugular venous blood samples were obtained just before and 30 min and 24 h after anaesthesia. Samples were kept in EDTA test tubes for haematological analyses and in vacutainer tubes for biochemistry. Red blood cells (RBC), white blood cells (WBC), packed cell volume (PCV) and haemoglobin (Hb) were quantified with the Hematil–2000 cell counter. The amount of MDA, the end-product of polyunsaturated fatty acid peroxidation, in the serum was determined (Satoh, 1978; Yagi, 1984). Erythrocyte GSH-Px, catalyzing the formation of the oxide glutathione (GSSG), was measured (Beutler, 1975) and the concentration of NADPH, a cofactor required for the action of glutathione reductase (GSH-az) and the formation of cumene hydroperoxide, was measured at 340 nm using a spectrophotometer (Shimadzu 2R/UV–Vis) (Beutler, 1975). The levels of serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), glucose, calcium (Ca), phosphorus (P), sodium (Na), potassium (K), and chloride (Cl) were measured with an autoanalyser (Technicon RA-XT). Student's t test was used to calculate the differences between the values of the groups.

Mean values of the investigated parameters in samples taken immediately before, 30 min and 24 h after anaesthesia are presented in Table 1. We observed a significant increase in the levels of glucose ($P < 0.001$), GSH-Px ($P < 0.05$), and MDA ($P < 0.05$) during anaesthesia. Although, there was some decrease in the levels of all four haematological parameters (RBC, WBC, PCV, Hb) we measured, the differences were not statistically significant. Similarly, we observed a slight decrease in the levels of phosphorus but this was also not significant. The other parameters (AST, ALT, Ca, Na, K, and Cl) did not display any obvious changes (Table 1).

Acute hyperglycaemia and hypoinsulinaemia have been reported in cattle given i.v. xylazine, reflecting the inhibition of insulin release from the pancreatic β cells by the α_2-adrenaergic receptors (Hsu and Hummel, 1981; Lumb and Jones, 1996). Moreover, the level of glucose was increased in dogs anaesthetised with enflurane (Naziroğlu and Gunay, 1999). Şindak (2001) showed similar results in dogs anaesthetised with a tiletamin–zolazepam–xylazine combination.

Khinev et al. (1995) reported in humans that there was no significant change in MDA levels before and after anaesthesia. On the other hand, Naziroğlu and Gunay (1999) in dogs, and Neri et al. (1994) and Glantzounis et al. (2001) in humans showed an increased serum level of MDA during anaesthesia. Our data support the latter reports. Naziroğlu and Gunay (1999) reported that serum GSH-Px activity did not change significantly during anaesthesia, possibly because it was significantly lower than in erythrocytes and other tissues. In contrast, Neri et al. (1994) indicated an increase in the GSH-Px activity during anaesthesia. Our results also show a significant increase in the GSH-Px activity ($P < 0.05$).

Hb, RBC, and PCV values in cattle anaesthetised by xylazine were reported to decrease (Lumb and Jones, 1996) and Lagutchik et al. (1991) documented a signif-

Table 1
Changes in haematological parameters, enzymatic activities, glucose and ion levels before, 30 min and 24 h after anaesthesia in gazelles

	Before	During	After
Cells			
RBC × 10^6 (mm^3)	11.76 ± 0.05	9.14 ± 1.69	11.42 ± 0.45
WBC × 10^3(mm^3)	11.19 ± 3.24	8.41 ± 4.42	10.59 ± 1.99
PCV (%)	53.19 ± 6.28	47.51 ± 9.88	52.25 ± 4.74
Hb (g/L)	197.6 ± 19.3	176.9 ± 31.4	191.2 ± 11.9
Enzymes			
GSHPx (U/g Hb)	115.0 ± 27.7	188.6 ± 59.3*	94.6 ± 20.8
MDA (μmol/L)	2.58 ± 0.09	3.69 ± 0.07*	2.91 ± 0.15
AST (U/L)	372 ± 169	376 ± 177	368 ± 103
ALT (U/L)	50.0 ± 27.3	46.8 ± 26.6	48.2 ± 14.9
Glucose			
Glucose (mg/L)	620.0 ± 370.0	2024.0 ± 630.0**	750.0 ± 323.0
Ions			
Ca (mg/L)	91.0 ± 6.4	89.8 ± 6.3	91.5 ± 4.6
P (mg/L)	70.0 ± 10.1	54.3 ± 14.6	63.0 ± 5.8
Na (mmol/L)	154.86 ± 9.44	152.14 ± 7.86	153.19 ± 7.10
K (mmol/L)	5.11 ± 0.74	4.41 ± 0.83	4.78 ± 0.39
Cl (mmol/L)	113.29 ± 5.15	111.86 ± 4.88	110.36 ± 6.67

Results are expressed as mean ± SE. Statistically significant when compared to other groups with *$P < 0.05$ and **$P < 0.001$ values.

icant decrease in the Hb and PCV levels in sheep anaesthetised with tiletamin–zolazepam. Şindak (2001), however, indicated that the glucose level was significantly higher although some other biochemical and haematological parameters were not affected in dogs anaesthetised with tiletamin–zolazepam–xylazine.

In conclusion, a tiletamin–zolazepam–xylazine combination causes hyperglycaemia in gazelles. This may result in high oxidation stress, which may then lead to an increase in the levels of erythrocyte GSH-Px and serum MDA. Our result support the hypothesis that the use of anaesthetics such as tiletamin–zolazepam and xylazine may cause some oxidative stress in animals and should therefore be used cautiously both in veterinary clinics and research.

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