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Haemato - biochemical evaluation of detomidine in cattle

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Abstract
Haemato - biochemical evaluation of detomidine - a sedative drug, at different dose rates was studied in cattle. The study was conducted in 18 cattle. The cattle were randomly divided into 3 groups of 6 cattle each. 10, 20 and 30 µg/kg body weight detomidine given intravenously to the group I, II and III respectively. Haematological parameters like haemoglobin, total erythrocyte count, packed cell volume, total leucocyte count and differential count and biochemical parameters like plasma cortisol, blood glucose, total serum protein, aspartate aminotransferase, alanine aminotransferase, blood urea nitrogen and creatinine were studied. The data were collected before sedation, at peak sedation, after recovery and after taking feed and water. Total erythrocyte count, haemoglobin and packed cell volume values were reduced significantly at peak sedation. Total leucocyte count and differential count showed no significant change at any stage of the study. Blood glucose level increased significantly in a dose dependent manner at peak sedation and the increase continued upto after recovery. Plasma cortisol level was not induced by detomidine. Other parameters showed only non significant changes after detomidine administration.

Keywords: Detomidine, blood glucose, haemoglobin, total erythrocyte count, packed cell volume, plasma cortisol

1. Introduction
Detomidine - a very good, low cost sedative drug - alternative to xylazine (Gnanasekar *et al*., 2013) [4] is now commonly used in the field of veterinary surgery. It has a wide margin of safety (5 to 300 µg/kg body weight) as reported by Vainio (1985) [21] and also it does not cause abortion and regurgitation even in unfasted animals (Schatzmann *et al*., 1994) [17]. So the pregnant animals can be safely sedated with detomidine when needed. Lower doses can be very well used for standing sedation required for certain dignostic procedures and minor surgical procedures and the higher doses can be used for the other ruminant surgeries done with sedation alone (Gnanasekar *et al*., 2019) [5].
Hence, it was decided to study the haematological and biochemical parameters including stress parameter like plasma cortisol during different dose rates of detomidine sedation in cattle to find out its action on various vital organ functions including hepatic system and urinary system functions.

2. Materials and methods
18 cattle were randomly divided into 3 groups of 6 cattle each. 10, 20 and 30 µg/kg body weight detomidine administered intravenously to the group I, II and III respectively. Haematological parameters like haemoglobin (gm/dl), total erythrocyte count (10^6/cumm), packed cell volume (%), total leucocyte count (10^3/cumm) and differential count (%) were estimated as per the standard methods prescribed by Coles (1986) [3]. Biochemical parameters like blood glucose (mg/dl), total serum protein (gm/dl), aspartate aminotransferase (IU/L), alanine aminotransferase (IU/L), blood urea nitrogen (mg/100ml) and creatinine (mg/100ml) were estimated as per the standard methods prescribed by Kaneko *et al*. (1997) [6]. Plasma cortisol (ng/ml) levels were measured by competitive ELISA – ElAgen cortisol kit. The data were collected before sedation, at peak sedation, after recovery and after taking feed and water. The collected data were analysed using SPSS software package version 19 following ANOVA and students 't' test.

3. Results and Discussion
The results of the haematological analysis were given in table 1 and the biochemical analysis were given in table 2 and 3 respectively. Following detomidine sedation, the mean values of

haemoglobin, packed cell volume and total erythrocyte count decreased in all the groups. These changes could be attributed to the temporary haemodilution due to fluid shift from the extra vascular compartment into the vascular space to maintain cardiac output. In addition to this splenic sequestration of circulating erythrocytes due to decreased sympathetic stimulation (Wagner *et al.*, 1991 and Kullmann, 2011) [23, 8] also resulted in reduced total erythrocyte count, haemoglobin and packed cell volume. These findings concurred with the results of Lacerda *et al.* (2010) [12], Monsang (2011) [13], Khattri *et al.* (2013) [7] and Tiburcio *et al.* (2014) [20]. The mean values returned to base after taking feed and water in all the animals revealing that these changes were only transient.

Table 1: Mean ± SE values of Total erythrocyte count, Haemoglobin, Packed cell volume and Total leucocyte count

Parameters	Group	Before sedation	At peak sedation	After total recovery	After taking feed and water
Total erythrocyte count (10^6/cumm)	I	6.91^{b} ± 0.06	6.20^{a} ± 0.25	6.82^{b} ± 0.21	6.96^{b} ± 0.15
	II	8.25^{b} ± 0.26	7.43^{a} ± 0.26	8.49^{b} ± 0.26	8.20^{b} ± 0.16
	III	7.53^{b} ± 0.23	6.88^{a} ± 0.23	7.42^{b} ± 0.29	7.55^{b} ± 0.32
Haemoglobin (gm/dl)	I	11.26^{b} ± 0.26	9.73^{a} ± 0.34	10.81^{b} ± 0.24	11.05^{b} ± 0.31
	II	10.94^{b} ±.0.73	9.52^{a} ± 0.22	10.53^{b} ± 0.22	10.84^{b} ±0.24
	III	10.33^{b} ± 0.42	9.04^{a} ± 0.47	9.97^{b} ± 0.39	10.21^{b} ± 0.37
Packed cell volume (%)	I	34.68^{b} ± 0.75	28.57^{a} ± 0.71	32.4^{b} ± 0.63	33.90^{b} ± 0.58
	II	33.49^{b} ± 1.99	27.36^{a} ± 2.03	31.68^{b} ± 1.47	32.87^{b} ± 2.06
	III	33.89^{b} ± 1.59	28.95^{a} ± 2.74	31.07^{b} ± 2.52	32.95^{b} ± 2.55
Total leucocyte count (10^3/cumm)	I	9.27 ± 0.83	9.85 ± 0.39	9.56 ± 0.36	9.37 ± 0.40
	II	9.74 ± 0.56	10.42 ± 0.72	10.29 ± 0.58	9.91 ± 0.60
	III	9.81 ± 0.83	10.64 ± 0.87	10.48 ± 0.84	10.03 ± 0.93

Means bearing different superscripts in a row differ significantly (P<0.01)

The total leucocyte count increased after sedation in all the three groups. During sedation with detomidine a non significant decrease in the lymphocytes with corresponding neutrophilia could be noticed. The leucocytosis with neutrophilia and lymphopenia during detomidine sedation could be attributed to stress (Wagner, 1991) [22] induced changes associated with the changes in cardiopulmonary functions rather than the stimulation of hypothalamo-pituitary-adrenocortical axis as detomidine was devoid of hypothalamo-pituitary-adrenocortical axis stimulation (Taylor and Watkins, 1992) [19]. Leucocytosis with neutrophilia and lymphopenia was reported as the classical stress leucogram (Steffey *et al*., 1979) [18]. The non-significant increase in the leucocytic count with lymphopenia and corresponding neutrophilia in the present study could be attributed to the less stress induced by detomidine (Taylor and Watkins, 1992) [19]. Kumar *et al*. (2010) [11] attributed these changes to the pooling of circulating blood cells in spleen or other reservoirs secondary to decrease sympathetic activity, adrenocortical stimulation and subsequent effect of glucocorticoids (Lacerda *et al*., 2010 and Tiburcio *et al*., 2014) [12, 20]. Similar findings were reported in dogs (Ahmad *et al*., 2011) [1] and sheep (Monsang, 2011) [13] after administration of dexmedetomidine.

Table 2: Mean ± SE values of Blood glucose, Plasma cortisol and Total serum protein

Parameters	Group	Before sedation	At peak sedation	After total recovery	After taking feed and water
Blood glucose mg/100ml	I	60.95^{a} ± 3.15	70.83^{c} ± 2.33	75.29^{d} ± 2.19	67.18^{b} ± 3.62
	II	58.32^{a} ± 2.71	72.69^{c} ± 2.64	78.36^{d} ± 2.62	66.34^{b} ± 3.43
	III	56.91^{a} ± 3.95	75.17^{c} ± 2.74	80.03^{d} ± 2.70	66.07^{b} ± 3.57
Plasma cortisol ng/ml	I	8.93 ± 0.73	7.73 ± 1.09	8.00 ± 1.47	8.56 ± 1.11
	II	8.15 ± 0.67	7.25 ± 0.83	7.80 ± 1.10	8.01 ± 0.91
	III	8.66 ± 0.79	7.88 ± 0.90	8.21 ± 1.07	8.56 ± 0.76
Total serum protein gm/dl	I	6.82 ± 0.05	6.51± 0.06	6.43± 0.05	6.61± 0.05
	II	7.03 ± 0.06	6.77 ± 0.06	6.69 ± 0.05	6.83 ± 0.06
	III	7.52 ± 0.08	7.01 ± 0.04	6.87 ± 0.09	7.44 ± 0.06

Means bearing different superscripts in a row differ significantly (P<0.01)

The mean blood glucose level significantly increased after sedation in all the groups and it remained elevated after recovery and after taking feed and water. The increase was directly proportional to the dose of detomidine. The hyperglycemia due to the administration of α_2 -adrenergic agonist was attributed to increased hepatic glucose production (Kumar and Thurmon, 1979) [9], increased glucagon level and hypoinsulinemia (Brockmen, 1981) [2] mediated by adrenergic receptors in the cells of pancreatic islets (Kumar *et al*., 2010) [11]. Further, due to the hyperactivity of adrenal cortex resulting in glycogenolysis, decreased glucose utilization (Kumar *et al.*, 1974) [10], decreased membrane transport of glucose (Roy and Uppal, 1987) [16] and decreased renal excretion (Kumar *et al*., 1974) [10] and these were the additional factors which induced hyperglycemia. Detomidine as it was devoid of hypothalamo pituitary adreno cortical axis stimulation action (Taylor and Watkins, 1992) [19], the hyperglycemia could be attributed to the hypoinsulinemia. The hypoinsulinemia was attributed to the direct action on beta cells of pancreas and inhibition of oxidation of glucose (Khattri *et al*., 2013) [7].

Table 3: Mean ± SE values of Alanine aminotransferase, Aspartate aminotransferase, Blood urea nitrogen and Creatinine

Parameters	Group	Before sedation	At peak sedation	After total recovery	After taking feed and water
Alanine aminotransferase IU/L	I	10.82 ± 1.08	11.39 ± 1.16	11.14 ± 1.20	10.98 ± 1.20
	II	11.37 ± 1.65	12.08 ± 1.70	11.85 ± 1.65	11.56 ± 1.63
	III	10.05 ± 1.77	10.86 ± 1.83	10.63 ± 1.81	10.38 ± 1.47
Aspartate aminotransferase IU/L	I	29.50 ± 2.22	31.06 ± 2.53	31.52 ± 2.46	29.62 ± 2.38
	II	27.81 ± 2.82	30.54 ± 2.92	30.86 ± 3.04	27.98 ± 2.88
	III	31.24 ± 3.49	33.98 ± 2.32	34.47 ± 2.17	31.57 ± 2.28
Blood urea nitrogen mg/100ml	I	8.01 ± 1.03	8.82 ± 1.06	9.03 ± 1.13	8.35 ± 1.08
	II	8.64 ± 1.20	9.68 ± 1.19	9.95 ± 1.38	8.99 ± 1.25
	III	8.32 ± 1.35	9.57 ± 1.49	9.86 ± 1.32	8.78 ± 1.16
Creatinine mg/100ml	I	1.03 ± 0.20	1.18 ± 0.22	1.23 ± 0.16	1.06 ± 0.20
	II	0.97 ± 0.18	1.19 ± 0.21	1.28 ± 0.22	1.08 ± 0.20
	III	1.24 ± 0.23	1.50 ± 0.28	1.69 ± 0.31	1.35 ± 0.26

In all the groups, plasma cortisol level decreased non significantly after detomidine administration. This was in concurrence with detomidine did not influence the cortisol level in horses (Raekallio *et al.,* 1991) [15] and there was a significant reduction in cortisol level in horses due to reduction in sympatho-adrenal activity (Raekallio *et al.,* 1992) [14].

There was a non significant reduction of total serum protein levels in all the animals noticed aduring sedation. Hypoproteinemia following α_2 -adrenergic agonists administration was reported by Tiburcio *et al*. (2014) [20]. Kumar *et al*. (2010) [11] attributed the increased levels of glucocorticoids, adrenal activity and increased protein turn over resulting in decreased plasma protein and albumin. It may also be due to the impairment of general metabolism and impaired synthesis of protein, decreased insulin level and increased adrenal steroids.

At peak sedation the alanine aminotransferase and aspartate aminotransferase values increased non significantly. This showed that the drug did not cause any significant damage in liver. The findings concurred with Tiburcio *et al*. (2014) [20].

At peak sedation blood urea nitrogen and creatinine levels increased insignificantly in all the groups. The mean values fluctuated within the clinical levels during the period of study revealing that the drugs did not cause any impairment in glomerular filtration or renal blood flow. The findings concurred with Tiburcio *et al*. (2014) [20].

4. Conclusion

With all that haemato biochemical data evaluated in this study, detomidine did not cause any significant change with the vital organ functions, hence the drug can be used safely used at different dose levels according to the situation without any complications.

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