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HAEMATO-BIOCHEMICAL RESPONSE TO XYLAZINE-PROPOFOL ANAESTHESIA AND ITS REVERSAL BY YOHIMBINE AND ATIPAMEZOLE IN DOGS

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ABSTRACT
Ten healthy mongrel dogs of either sex, weighing 10-20kg were divided into two groups of 5 animals each. In both the groups, animals were sedated with xylazine @1mg/kg I/M which was followed 10 min. later by propofol @ 4mg/kg intravenously. The haematological and biochemical effects of xylazine-propofol were completely reversed in group I by yohimbine @ 125 µg/kg I/V and in group II by atipamezole @ 100 µg/kg I/V 20 min. post xylazine-propofol anaesthesia. The haematological parameters *viz*., Hb, PCV and TEC showed non-significant decrease while non significant increase in TLC in both groups was recorded after anaesthesia which remained unaffected after reversal. Biochemical parameters *viz*. glucose, AST, ALT showed significant ($P<0.01$) increase after xylazine-propofol anaesthesia in both groups. BUN and creatinine showed significant ($P<0.01$) increase in group I however the increase was non-significant in group II. But after injection of reversal agents yohimbine and atipamezole these values decreased upto 15 min. post reversal. Thus, transient changes in the haemato-biochemical parameters were reversed to near normalcy after injection of reversal agents.

KEYWORDS: Atipamezole, Dogs, Propofol, Reversal, Xylazine, Yohimbine.

INTRODUCTION

Xylazine is centrally acting α_2-adrenergic receptor agonist with potent sedative, analgesic and muscle relaxant activity which is commonly used in canine surgery either alone or in combination with other sedative, analgesic or anaesthetic agents (Booth, 1992). Propofol is an ultra shorting acting, non-barbiturate, non-dissociative intravenous anesthetic agent which is used to induce and maintain anaesthesia in dogs (Kilic, 2004). Duration of anaesthesia is 10 minutes and complete recovery occurs in 25-30 minutes. Muscle relaxation is excellent and degree of analgesia is suitable for minor surgical procedures (Genevois *et al*., 1988). But being poor analgesic, it must be supplemented with an analgesic agent such as opioids or α_2-agonists if it is used to maintain anaesthesia. For reversing xylazine-induced CNS depression, bradycardia and tachypnea, among α_2-adrenoceptor antagonist, yohimbine and atipamezole have been commonly used (Hall and Clarke, 2001). Therefore, an antagonist would be beneficial to safeguard the use of xylazine as they hasten arousal time and increase the margin of safety. The present study was conducted to observe the haematological and biochemical response to xylazine-propofol anaesthesia and its reversal by yohimbine and atipamezole in dogs.

MATERIALS & METHODS

Ten healthy mongrel dogs of either sex, weighing 10-20 kg and were divided into two groups of 5 animals in each. Prior to start of the experiment, each dog was starved for 12 hour and water was withheld for 2 hour. In both the groups, all the animals were sedated with xylazine@ 1mg/kg I/M which was followed 10 min. later by propofol @4mg/kg intravenously. After 20min. xylazine- propofol anaesthesia, the haematological and biochemical effects were reversed in group I by yohimbine @125 µg/kg and in group II by atipamezole @ 100 µg/kg intravenously. The blood/ serum samples were collected from the experimental animals before (0 min.), 20 min. post xylazine-propofol anaesthesia and at 15 and 60 min. post reversal for estimation of haematological and biochemical parameters. The mean and standard error of recorded values were calculated. The data was analyzed as per the standard procedure outlined by Snedecor and Cochran (1967).

RESULTS & DISCUSSION

The alpha$_2$-adrenoceptor agonist and antagonists hold promise for the anaesthetist because they can mediate analgesia, anxiolysis, sedation, sympatholysis and control of hypertension. One of the most significant advances in Veterinary anaesthesiology during the last decade was the utilization of antagonist for the reversal of injectable anaesthetic regimens. The haematological and biochemical parameters after xylazine-propofol anaesthesia and after its reversal with yohimbine or atipamezole in both groups of animals at various intervals are given in Table 1 and Table 2, respectively. Haemoglobin showed a non-significant decrease at 20 min. after xylazine-propofol anaesthesia in both groups of animals. The decrease in haemoglobin level might be due to pooling of blood cells in the spleen induced by adrenolytic property of α_2-agonists. Similar findings have been reported by Lim *et al*. (2000) and Couto (2003) in dogs. In animals of group I

and II, after injection of yohimbine and atipamezole respectively, a non-significant increase in Hb level at 15 min. was recorded which, returned to near preadministration level by 60 min. post reversal. Similar response has been seen after injection of yohimbine in xylazine-pentobarbital anaesthesia by Mc Gruder and Hsu (1985) in ponies. The values ranged between 10.9±0.40 gm % to 13.52 ±0.47 gm % at various intervals in both the groups. The packed cell volume showed non-significant decrease 20 min. post xylazine-propofol anaesthesia in both groups of animals. After administration of reversal agents *viz*. yohimbine or atipamezole in group I and II, PCV non-significantly increased upto 15 min. post reversal and returned to pre-administration level by 60 min. Mc Gruder and Hsu (1985) have reported similar observations in ponies after administration of yohimbine to counter act xylazine-pentobarbital anaesthesia. The PCV values ranged from 39.2 ±0.57 % to 42.4 ±0.67 %. The total erythrocyte count (millions/mm^3) showed non-significant decrease 20 min. post xylazine-propofol anaesthesia in both groups of animals. This might be due to pooling of red blood cells in the spleen during early stage of anaesthesia. Similar findings were observed by Ozaydin *et al*. (2001) and Jain *et al*. (2004) in dogs. In group I and II, increase in the TEC level was observed at 15 min. after injection of yohimbine or atipamezole respectively and it returned to near preadministration level by 60 min. post reversal. The TEC values ranged from 5.74 ±0.35 millions/mm^3 to 6.46 ±0.16 millions/mm^3. A non-significant increase in TLC was observed after 20 min. xylazine-propofol anaesthesia in both groups. After injection of yohimbine or atipamezole in group I and II respectively, there was further a non-significant increase 15 min. post reversal which returned to near control values 60 min. post reversal. The transient increase in TLC after anaesthesia could be attributed to stress and release of ACTH on account of their administration. Similar findings have also been reported by Gill *et al*. (1996) in dogs. The TLC values ranged from 11.35± 0.44 thousands / mm^3 to 13.2 ± 0.71 thousands / mm^3 in both groups.

Serum glucose showed a significant (P<0.01) increase at 20 minutes after xylazine-propofol anaesthesia in both the groups of animals. The rise in glucose level might be due to activation of alpha$_2$-adrenoceptors present in the beta cells of pancreatic islets exerting a negative control of basal insulin release. After administration of reversal in both the groups, the glucose level decreased at 15 min. and however, the values returned near preadministration level by 60 min. after reversal. Significant hyperglycaemias induced by xylazine-propofol anaesthesia become lesser after intravenous administration of yohimbine or atipamezole. Similar observations have also been reported by Gogoi *et al*. (2002) in goats and Tiwari *et al*. (1998) in buffaloes. The mean serum glucose values ranged from 88.7 ±0.65 mg/dl to 102.94 ±1.42 mg/dl. There was a significant (P<0.01) difference in serum glucose level between both groups at various intervals. In the present study, the increased glucose concentration was partially controlled which might be due to injection of minimum effective doses of yohimbine or atipamezole that caused dose dependent reversal of xylazine-propofol anaesthesia. Total serum proteins showed a non-significant decrease at 20 min. post xylazine-propofol anaesthesia in different groups of animals. The decrease in total proteins might be due to haemodilution or secondary elevation of globulins. After administration of yohimbine or atipamezole, total serum proteins non-significantly increased by 15minutes and returned to near normalcy by 60 min. post reversal. Similar observations have also been reported by Amarpal and Kumar (1995) in bovines and Gogoi *et al*. (2002) in goat. In the present study, progressive return of total proteins to normalcy might be due to reversal of α_2-adrenoceptor activation induced haemodilution by yohimbine or atipamezole. The values ranged from 4.72 ±0.11 gm/dl to 5.26 ±0.06 gm/dl. There was a non-significant difference in total serum proteins level between both groups of animals reversed with yohimbine or atipamezole at various intervals.

The SUN values showed a significant (P<0.01) increase at 20 min. post xylazine-propofol anaesthesia in group I and a non-significant increase in group II. The mean SUN values ranged from 20.2 ±0.37 mg/dl to 24.42 ±0.38 mg/dl at various intervals in both groups. The reversal with yohimbine and atipamezole in group I and II caused a non-significant decrease in the SUN level at 15 min. after injection. However, the values returned to preadministration level by 60 min. There was a significant (P<0.01) difference in SUN values between groups at various intervals. The values of creatinine showed a significant (P<0.01) increase at 20 min. post xylazine-propofol anaesthesia in group I where as in group II there was a non-significant increase in the creatinine values. After reversal with yohimbine or atipamezole, the creatinine level returned close to pre-administration level by 60 minutes in group I and II. The maximum increased value of 1.98 ±0.03 mg/dl (control value1.37 ±0.01 mg/dl) and 1.53 ±0.04 mg/dl (control value 1.44 ±0.01 mg/dl) were recorded in group I and II respectively at 20 min. post anaesthesia. There was a significant (P<0.01) difference in the serum creatinine values between groups at various intervals. An increase in SUN and creatinine levels after xylazine-propofol anaesthesia decreased progressively and returned to preadministration level by 60 min. after intravenous injection of yohimbine and atipamezole. These findings have also been supported by Raekallio *et al*. (1991) in calves and Gogoi *et al*. (2002) in goats. In the present study, administration of yohimbine and atipamezole slightly affected the rising trend and return to pre-administration level, which might be due to the antagonistic effect of reversal agents on xylazine.

Serum AST showed a significant (P<0.01) increase at 20 min. post xylazine-propofol anaesthesia in both the groups of animals. The reversal with yohimbine and atipamezole administration caused a significant (P<0.01) decrease in AST values which returned near pre-administration level by 60 min. after reversal. There was a significant (P<0.01) variation in serum AST values between groups of animals at various intervals. Serum ALT showed a highly significant (P<0.01) increase at 20 min. post xylazine-propofol anaesthesia in group I and a significant (P<0.05) increase in group II which decreased but still remained significantly (P<0.01) high after reversal with yohimbine or atipamezole and returned to near pre-administration level by 60 min. Similar observations have also been

reported by Mc Gruder and Hsu (1985) in ponies and Tiwari *et al*. (1998) in buffalo calves. The progressive return of serum enzymes to pre-administration level might be attributed to effective antagonism of α_2-agonist after injection of yohimbine and atipamezole. The ALT values ranged from 27.08 ±0.20 U/L to 31.5 ±0.40 U/L in both the groups at various intervals. The maximum values recorded in group I was 30.5 ±0.16 U/L (control value 28.00 ±0.12 U/L) and 31.5 ±0.40 U/L (control value 30.25 ±0.37 U/L) in group II. There was a significant (P<0.01) variation in serum ALT values between groups of animals at respective intervals. Thus, transient changes in haemato-biochemical parameters were reversed to near normalcy after injection of reversal agents. It was concluded that xylazine-propofol anaesthesia could be safely used in dogs and the reversal agents minimizes the post-anaesthetic recumbency and thus increases the margin of safety.

TABLE 1. Effect on haematological parameters after xylazine- propofol anaesthesia and after its reversal at various intervals in dogs (Mean ±S.E.)

Parameters	Groups (n=5)	0 min.	20 min. post xylazine-propofol anaesthesia	Post Reversal (minutes)	
				15	60
Hb (gm/dl)	I	13.32±0.34	12.34±0.62	13.08±0.80	13.52±0.47
	II	11.96±0.54	10.9±0.40	12.06±0.25	12.26±0.35
PCV (%)	I	41.2±0.65	39.2±0.57	41.8±0.60	41.5±0.54
	II	41.8±0.76	39.4±0.45	42.2±0.59	42.4±0.67
TEC ($\times 10^6$ cu mm^{-1})	I	6.38±0.28	5.74±0.35	6.08±0.318	6.30±0.24
	II	6.46±0.16	5.78±0.22	6.12±0.23	6.40±0.18
TLC ($\times 10^3$ cu mm^{-1})	I	11.8±0.25	12.42±0.32	13.2±0.71	11.35±0.44
	II	12.0±0.22	12.5±0.38	12.8±0.33	11.6±0.24

TABLE 2. Effect on biochemical parameters after xylazine-propofol anaesthesia and after its reversal at various intervals in dogs (Mean ± S.E.)

Parameters	Groups (n=5)	0 min.	20 min. post xylazine-propofol anaesthesia	Post Reversal (minutes)	
				15	60
Glucose (mg/dl)	I	93.00±0.85	102.94±1.42**	101.5±0.73**	95.4±0.67
	II	87.03±0.52	98.29±0.69**	91.3±0.93**	88.7±0.65
Total Serum Proteins (gm/dl)	I	5.19±0.06	5.02±0.54	5.14±0.50	5.26±0.06
	II	4.95±0.06	4.72±0.11	4.98±0.04	4.99±0.073
Serum Urea Nitrogen (mg/dl)	I	22.35±0.27	24.42±0.38**	22.38±0.27	22.12±0.36
	II	20.2±0.37	21.40±0.48	21.26±0.42	20.43±0.51
Creatinine (mg/dl)	I	1.37±0.01	1.98±0.03**	1.49±0.06	1.09±0.06**
	II	1.44±0.01	1.53±0.04	1.48±0.03	1.45±0.03
AST (U/L)	I	38.25±0.14	39±0.16**	37.6±0.18**	36.25±0.12
	II	41.4±0.24	42.60±0.20**	42.15±0.16**	42.25±0.27*
ALT(U/L)	I	28.00±0.12	30.5±0.16**	29.25±0.22**	27.08±0.20
	II	30.25±0.37	31.5±0.40*	31.00±0.29*	30.2±0.28

* P<0.05= Significant at 5% level as compared to zero minute value
**P<0.01= Significant at 1% level as compared to zero minute value

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