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LUMBOSACRAL EPIDURAL XYLAZINE HYDROCHLORIDE INJECTION PLUS CO-LOADING WITH LACTATED RINGERS SOLUTION: EFFECTS ON CARDIOVASCULAR AND HAEMATO-BIOCHEMICAL VARIABLES OF DOGS

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ABSTRACT

Objectives: **Epidural xylazine hydrochloride (Hcl) injection often leads to hypotension and haemto-biochemical alterations in dogs. Crystalloid fluid administration is advised to counter xylazine's hypotensive effect. Information is lacking concerning the effect of concomitant epidural Xylazine Hcl and lactated ringers administration on cardiopulmonary and haemato-biochemical parameters of dogs.**

Design: **The dogs were randomized into group 1 (Epidural Xylazine-EXY alone), group 2 (EXY co-loaded with LRS at the rate of 10 ml/kg/hour), group 3 (EXY + 20ml/kg/hr LRS), and group 4 (EXY + 30ml/kg/hr LRS). Co-loading with EXY was done immediately after lumbosacral epidural injection of 1 mg/kg xylazine Hcl. Subsequently, cardiovascular and haemato-biochemical changes were recorded before administration of xylazine and subsequently at 30, 90 and 180 minutes.**

Result: **Post treatment, pulse rate and heart rate decreased in all groups. Packed cell volume (PCV) of the groups decreased. Haemoglobin concentrations (Hbc) of the LRS treated groups did not differ significantly (P>.05) when compared with Hbc of EXY group. Erythrocyte sedimentation rates increased in all the groups but did not vary significantly between the groups (P>0.05). Increase in potassium concentration was recorded in all the groups while sodium concentrations decreased.**

Conclusion: **This study established that concomitant treatment with LRS did not further exacerbate the haematologic effects of epidural xylazine in dogs.**

INTRODUCTION

Epidural anaesthesia is one of the most versatile and extensively utilized regional anaesthetic technique in animals. Lumbosacral epidural anesthesia provides complete anesthesia to the caudal half of the body by blocking the intradural spinal nerve roots and the peripheral layers of the spinal cord (1). Epidural anaesthesia has been demonstrated to be effective for a variety of surgical procedures such as cesarean section (2), ovariohysterectomy (3) and soft tissue surgeries (4). This form of regional anesthesia has also been used in combination with general anesthesia to reduce anesthetic and analgesic requirements, improve analgesia, and quality of anesthetic recovery (5). It is also a very popular method of pain control for labouring parturients (6).

Fasting, disease, anaesthesia and surgery affects the body physiological capacity not only by altering its external fluid and electrolyte balance but also the body homeostasis (7). Xylazine, an alpha$_2$ adrenergic agonist is used as a sedative and analgesic in veterinary practice (8). They are also known to exhibit spinal cord alpha$_2$ adrenoceptor mediated analgesic effects (9). Based on this latter activity, xylazine hydrochloride had been used to induce epidural anaesthesia in dogs (7, 10), cats (11), cattle (12), goats (13) and horses (14). In all the previous animal species to which xylazine was administered epidurally, significant depression in cardiopulmonary function was reported. Alterations in packed cell volume, total erythrocyte count, haemoglobin concentrations, erythrocye sedimentation rate, total leucocyte count and platelet count as well as changes in some serum biochemical parameters of dogs during epidural xylazine anaesthesia has been previously documented (15).

The goal of fluid therapy in the elective setting is to maintain the effective circulatory volume while avoiding interstitial fluid overload (16). Other reasons for which fluid(s) is administered include replacement of sensible or insensible fluid losses, and replacement as well as maintenance of adequate cardiac output and tissue perfusion during the anaesthetic period (16). Decisions regarding whether to provide fluids during anaesthesia and the type to be used depends on the patient's signalments, physical condition and type of the procedure (17). In clinical practice, the most common complication of epidural anaesthesia is hypotension prompting fluid infusions or administration of vasopressors (18). Fluids of choice include crystalloids or colloids (19). Colloids are more expensive and have higher potential to cause allergic reactions compared to crystalloids (18). Thus, crystalloids remain the first choice of fluid for prevention of hypotension (20). In human patients undergoing caesarean section, at fluid infusion rates of 100-150 ml/min, the estimated median effective volume (EV_{50}) of lactated ringers required to prevent spinal anaesthesia- induced hypotension was approximately 13ml/kg (21). Unlike in humans, in dogs, there is dearth of information concerning the appropriate volume of lactated ringers solution needed to maintain the cardiovascular function during epidural xylazine anaesthesia.

The goal of this study was to ascertain the appropriate rate of lactated ringers for rapid volume expansion during lumbosacral epidural anaesthesia.

MATERIALS AND METHODS

Animals: Twelve (12) adult, male mongrel dogs weighing 5.5±0.2kg were used in the study. The dogs were kept in different cages under similar experimental conditions at the University of Nigeria Nsukka Veterinary surgery dog kennel house. They were provided with dog food (JO-JO®, France) two times daily while water was provided *ad libitum*. The animals were allowed to acclimatize for two weeks prior to the study. The protocols used for this research were approved by the Animal Ethics Committee, University of Nigeria, Nsukka (approval no. UNAEC/19/8251).

Anaesthesia and fluid therapy: The dogs were randomized into four (4) groups; group 1 (Epidural Xylazine-EXY alone), group 2 (EXY + 10ml/kg/hr LRS), group 3 (EXY + 20ml/kg/hr LRS), and group 4 (EXY + 30ml/kg/hr LRS). Injection of 1 mg/kg xylazine hydrochloride (xylazine 20®, Kepro, Holland) was made into the lumbosacral epidural space of dogs in the four groups. The epidural deposition was confirmed by lack of resistance to injection. The presence of analgesia was taken as lack of response to "pin pricking". Immediately after epidural injection of xylazine, lactated ringers solution was administered at rate of 10ml/kg/hr, 20ml/kg/hr and 30 ml/kg/hr to dogs in groups 2, 3 and 4 respectively.

Data collection: Cardiovascular variables: Heart and pulse rates of all dogs in the four groups were recorded before (baseline) administration of xylazine and subsequently at 30, 90 and 180 minutes using a Veterinary multi-parameter monitor TM-9009 (Technocare Medisystems, India).

Haemato-biochemical variables: Blood samples (5 ml) were collected from each animal before administration of xylazine and at 30, 90, and 180-minutes after administration of xylazine. Haemoglobin (Hb) concentration by the cyanohaemoglobin method, erythrocyte sedimentation rate (ESR) by the Wintrobe method and packed cell volume by the microhaematocrit method were analysed (22). Serum sodium, potassium, chloride and bicarbonate were assayed using kits manufactured by Quimica Clinica Applicada (QCA, Spain) under standard conditions. Serum pH was determined with the aid of a digital pH meter (Hanna Instrument Inc, USA).

Data analysis: The results were expressed as mean ± SEM. Mean cardiopulmonary, haematologic and biochemical parameter were analyzed using Multivariate analysis of Variance followed by LSD post hoc test for comparison of means between groups and within groups. Probability value less than 0.05 were considered significant.

RESULTS

Heart and pulse rates of dogs: After treatment, pulse rate and heart rate decreased in all groups. Compared to their baseline values, pulse rate and heart rates of groups 1, 2, 3 and 4 were significantly lower at 30 and 90 minutes. Mean pulse rate of group 4 was significantly ($P<0.05$) higher compared to pulse rate of the other groups at 90 minutes post treatment. Details are shown in Table 1.

Table 1

Cardioplumonary parameters (Mean ± SE) obtained in four groups (n=4) of dogs before and after lumbosacral epidural administration of xylazine HCL plus LRS

Parameters	TIME (MINUTES)	GROUPS			
		1(EXY)	2(EXY + 10ml/kg/hr LRS)	3(EXY + 20ml/kg/hr LRS)	4(EXY + 30ml/kg/hr LRS)
PR (beats/min)	0	118.67±3.33[a]	124.00±4.00[a]	121.33±3.53[a]	120.00±6.11[a]
	30	97.33±7.42[a*]	108±8.33[a*]	94.67±11.62[a*]	96.00±12.86[a*]
	90	88.00±4.62[a*]	89.33±5.81[a*]	98.67±3.53[a*]	108.00±6.93[b*]
	180	114.67±7.42[a]	120.00±2.31[a]	113.33±5.33[a]	118.67±3.53[a]
HR (beats/min)	0	116.00±6.11[a]	117.33±1.33[a]	112.00±8.33[a*]	118.67±3.53[a]
	30	78.67±4.81[a*]	78.67±4.81[a*]	82.67±4.81[a*]	92.00±2.31[a*]
	90	93.33±2.67[a*]	117.33±10.6[b*]	97.33±4.81[ab*]	96.00±4.00[ac*]
	180	128.00±2.31[a*]	129.33±4.81[a*]	126.67±2.67[a]	124.00±4.00[a]

EXY: epidural xylazine, LRS: lactated ringers solution, pH: potency of hydrogen, PR:pulse rate, HR: heart rate, RT: Rectal temperature

Different superscripts[a,b,c] in a row indicates significant difference (P<0.05) between means obtained in the four groups at different time intervals.

**values significantly different (P<0.05) from values recorded at baseline (t=0).*

Haematologic variables: As shown in Table, 2, packed cell volume (PCV) decreased in all groups following treatments. Post treatments, packed cell volumes of dogs in the respective groups at 30, 80 and 180 were significantly lower than baseline PCV values of the groups. Mean packed cell volumes of the EXY-LRS treated groups were not significantly (p>0.05) different from PCV of group 1 (EXY group) at 30, 90, and 180 minutes post treatment.

Haemoglobin concentration (Hbc) increased in all groups with the Hbc obtained at 90 minutes post treatment in all groups being significantly higher than their baseline Hbc values. Haemoglobin concentration obtained post treatment in the four groups when compared were not significantly (p>0.05) different. Erythrocyte sedimentation rate (ESR) of all the groups increased. Post treatment, at 90 and 180 min, ESR obtained in groups 1(EXY) was significantly higher than baseline ESR value of the group while significant increase in ESR of group 4 (EXY + 30 ml/kg/hr LRS) was recorded at 30 and 90 min. Comparison of ESR of the groups showed that they were not significantly different (p > 0.05) at 30-, 90-, and 180-minutes post treatment.

Table 2

Haematologic values (Mean ± SE) obtained in four groups (n=4) of dogs before and after lumbosacral epidural administration of xylazine HCL plus LRS

Parameters	TIME (MIN)	GROUPS			
		1 (EXY)	2(EXY + 10ml/kg/hr LRS)	3 (EXY +20ml/kg/hr LRS)	4 (EXY + 30 ml/kg/hr LRS)
PCV (%)	0	40.00±2.31[a]	43.67±1.86[a]	45.00±2.65[a]	40.00±2.31[a]
	30	22.33±2.03[a*]	25.67±5.21[a*]	25.67±3.18[a*]	25.00±2.31[a*]
	90	24.67±4.81[a*]	26.00±3.21[a*]	27.33±6.23[a*]	27.00±3.79[a*]
	180	17.67±1.86[a*]	23.00±3.06[a*]	24.67±8.00[a*]	28.00±2.00[a*]
Hb(g/dl)	0	10.28±1.08[a]	9.51±1.21[a]	9.62±1.28[a]	10.28±1.08[a]
	30	11.41±1.92[a]	11.36±2.58[a*]	13.90±1.75[a*]	11.14±1.15[a]
	90	12.84±0.84[a*]	14.03±1.87[a*]	11.19±1.79[a*]	12.79±0.97[a*]
	180	10.17±0.98[a]	10.50±1.41[a]	12.16±1.52[a*]	11.42±0.73[a]
ESR (mm/hr)	0	0.07±0.07[a]	0.07±0.63[a]	0.10±0.00[a]	0.07±0.07[a]
	30	0.22±0.10[a]	0.07±0.33[a]	0.11±0.44[a]	0.20±0.06[a*]
	90	0.30±0.06[a*]	0.10±0.06[a]	0.11±0.04[a]	0.18±0.16[a*]
	180	0.17±0.12[a*]	0.13±0.13[a]	0.18±0.11[a]	0.17±0.05[a]

EXY: epidural xylazine, LRS: lactated ringers solution, PCV: Packed cell volume, Hb: Haemoglobin concentration, ESR: erythrocyte sedimentation rate

Different superscripts[a,b,c] in a row indicates significant difference (P<0.05) between means obtained in the four groups at different time intervals.

**values significantly different (P<0.05) from values recorded at baseline (t=0).*

Biochemical variables: As shown in table 3, post lumbosacral epidural xylazine administration plus LRS infusion, significant (P<0.05) increase in potassium concentration occurred in EXY group and EXY+LRS groups. Potassium concentration obtained in group 1 (EXY) at 30 and 90 min after administration of treatment were significantly (P<0.05) higher than potassium concentration s in groups 2, 3 and 4 (EXY+ LRS groups). Serum sodium levels of all the groups decreased between 30 to 90 minutes after treatment. However, sodium level obtained in groups 2 and 3 at all-time points after treatment were not significantly lower (P>0.05) than their baseline values. In group 1 which received epidural xylazine injection alone, between 90 and 180 minutes, sodium level obtained were significantly (P<0.05) lower than the baseline sodium level. Also, in group 4 treated with EXY + 30 ml/kg/hr LRS, sodium level obtained at 90 minutes was significantly lower than the baseline value. Comparison of sodium values obtained in the four groups showed that sodium concentration of group 4 was significantly (p<0.05) higher than sodium levels of groups 1, 2, and 3 at 180 minutes post treatment.

Bicarbonate level increased after treatment with EXY and EXY + 10 ml/kg/hr LRS but decreased after treatment with EXY + 20ml/kg/hr LRS and EXY + 30ml/kg/hr LRS. When compared, there was no significant difference (p> 0.05) in mean bicarbonate concentrations of groups 1, 2, 3 and 4 at all-time intervals post treatment.

In all the groups pH decreased post treatment. In groups 3 and 4, pH obtained between 30, 90 and 180 minutes were significantly lower than 0 min pH while pH of group 2 was lower than its baseline at 30 and 180 minutes. The pH of group 4 was

significantly lower ($p<0.05$) than pH of other groups at 30- and 90-minutes post treatment.

Table 3

Serum biochemical values (Mean ± SE) obtained in four groups (n=4) of dogs before and after lumbosacral epidural administration of xylazine HCL plus LRS

Parameters	TIME (MIN)	GROUPS			
		1 (EXY)	2(EXY +10ml/kg/hr LRS)	3 (EXY +20ml/kg/hr LRS)	4(EXY + 30 ml/kg/hr LRS)
Potassium(mEq/L)	0	5.2 ± 0.19[a]	4.28±0.49[a]	4.85±0.42[a]	5.2±0.19[a]
	30	7.37±1.16[a*]	4.42±0.19[bc]	4.71±0.7[bc]	5.31±0.52[c]
	90	6.52±1.07[a]	5.91±0.66[a*]	5.08±0.28[b]	5.34±0.16[a]
	180	5.76±0.37[a]	5.89±0.58[a*]	4.14± 0.72[b]	5.16± 0.16[a]
Sodium(mEq/L)	0	137.22 ± 19.61[a]	114.66 ± 20.72[a]	112.77± 12.68[a]	137.23 ± 19.61[a]
	30	116.82 ± 13.08[a]	99.64 ± 2.52[a]	107.01± 25.23[a]	121.67 ± 3.32[a]
	90	103.60 ± 8.54[a*]	91.66 ± 10.42[a]	95.32 ± 9.53[a]	99.50 ± 19.73[a*]
	180	108.73 ± 11.63[a*]	105.58 ± 5.22[ab]	103.15 ± 0.59[ab]	138.40± 13.37[c]
Bicarbonate(mEq/L)	0	29.29±1.90[a]	30.38±4.11[a]	35.41±0.76[a]	29.29±1.90[a]
	30	32.83±3.24[a*]	31.37±3.11[a]	30.88±4.59[a]	26.28±1.95[a]
	90	29.70±1.02[a]	35.03±2.24[a]	22.95±1.40[b*]	27.43±4.75[a]
	180	25.36±2.43[a*]	30.44±3.15[a]	26.50±1.98[a*]	23.66±1.04[a*]
pH	0	5.87±0.09[a]	6.00±0.06[a]	5.77±0.35[a]	5.87±0.08[a]
	30	5.83±0.27[a]	5.63±0.09[ab*]	5.17±0.07[ab*]	5.00±0.15[b*]
	90	5.40±0.31[a*]	5.83±0.19[a]	4.97±0.03[ab*]	5.38±0.02[b*]
	180	5.37±0.19[a*]	5.40±0.17[a*]	5.07±0.18[a*]	5.10±0.15[a*]

EXY: Epidural xylazine, LRS: Lactated ringers solution, pH: potency of hydrogen

Different superscripts[a,b,c] in a row indicates significant difference (P<0.05) between means obtained in the four groups at different time intervals.

**values significantly different (P<0.05) from values recorded at baseline (t=0).*

DISCUSSION

Cardiovascular depression characterized by hypotension or bradycardia is a known sequel of epidural xylazine anaesthesia in animals. In this study, marked decrease in heart and pulse rates occurred in all groups between 30 and 90 minutes post xylazine administration. In some previous studies, similar decrease in pulse rate were recorded after epidural xylazine administration in cattle (12), sheep (23), goats (24) and dromedary camels (25). Similarly, Mwanji *et al*. (10) reported marked decrease in heart rates (bradycardia) in dogs post xylazine epidural injection. Hypotension primarily occurs due to blockade of sympathetic nervous system which ultimately leads to arterial and venous vasodilation (26). In addition, bradycardia which occurs following epidural xylazine injection was attributed to several factors including decreased sympathetic outflow from the central nervous system, inhibition of nor-epinephrine release from sympathetic nerve terminals, direct depression of cardiac pacemaker and increased vagal tone (10).

Intravenous administration of fluids is one of the measures employed clinically during epidural anaesthesia to decrease the incidence of severe cardiovascular depression or

bradycardia which may ultimately result in hypotension. It is therefore common practice to infuse large volumes of 0.9% saline or lactated ringers (LRS) to achieve rapid volume expansion aimed at averting the incidence of hypotension during epidural block (26). In this study, it was expected that co-loading with LRS at the rates infused in this study would be effective, but this was not the case since pulse and heart rates of dogs decreased significantly post treatment. Therefore, it can be concluded that LRS at the rates infused could not effectively produce adequate volume expansion needed in the experimental dogs.

A notable side effect of rapid volume expansion is haemodilution at the expense of oxygen delivery (27). Haematology showed that PCV of all dogs in the four groups were significantly lower than their respective baseline values after xylazine injection and LRS infusion. Previously, significant decrease in the PCV of species given xylazine epidurally had been documented (15). Factors described as being responsible for this finding after xylazine administration included sequestration of blood cells in spleen and lungs (28) and shifting of fluid from extravascular to intravascular compartment in an attempt to maintain normal cardiac output in anaesthetized animal (29). Comparison of the mean PCV of the four groups showed that they were not significantly different. Therefore, the similar drop in PCV of dogs recorded in both EXY group and XYL+LRS groups, suggests that this side effect of xylazine was not exacerbated due to co-administration of xylazine and LRS infusion

Erythrocyte sedimentation rates (ESR) of dogs in all the groups' increased post-xylazine administration. Also, ESRs of groups given LRS at different rates were not significantly different with that of the control group. In two earlier studies, ESR increased significantly after epidural administration of xylazine hydrochloride in dogs (15) and buffalo calves (30). Red cells outside the body precipitate due to the higher density than plasma (31). Therefore, ESR increase as noted in this study might be either an effect of xylazine or was induced by stress.

Serum biochemical assay showed that while sodium decreased, potassium concentration of dogs increased. Animal studies have shown that infusion of large volumes of LRS decreased serum sodium concentration and osmolality (32). Thus the recorded drop in serum sodium concentration and the compensatory increase in potassium concentration suggests that concomitant use of xylazine and LRS may cause marked reduction in serum osmolality. This may be the reason for the higher potassium concentration of EXY group as against potassium concentrations of EXY+LRS groups in the immediate periods post treatment.

Blood pH and bicarbonate levels of the groups reduced. Commercially available LRS has a pH of approximately 6.5 (33). Its infusion has been shown to cause increase in blood pH (33) probably due to conversion of lactate to bicarbonate. Based on these reports the change in pH and bicarbonate levels as observed in this study cannot be explained.

CONCLUSION

This study showed that co-loading with LRS at 10ml/kg/hr, 20 ml/kg/hr and 30 ml/kg/hr did not effectively produce adequate volume expansion needed to counter the cardiovascular effect of epidurally administered xylazine hydrochloride. Concomitant treatment with LRS did not further exacerbate the haematologic effects of epidural xylazine. However, serum sodium

concentrations may significantly decrease in dogs infused with LRS during epidural xylazine anaesthesia.

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