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Hematochemical Changes Following Epidural Analgesia by Bupivacaine, Ketamine and Their Combination in Chall Sheep

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Abstract: One of the most common ways of analgesia in small ruminants, especially sheep, is epidural method. Various agents are used in sheep. The objective of this study, is to evaluate effects of three analgesic agents, Bupivacaine (B), Ketamine (K) and their combination (BK), on some of the hematochemical parameters in Chall sheep following caudal epidural injection. Nine healthy Chall sheep (4 males, 5 females) with mean weight of 38.89±15.12 kg and aged 12-24 months were selected randomly and divided into three groups. The animals in group I received 0.5 mg kg^{-1} bupivacaine, in group II received 2.5 mg kg^{-1} ketamine and in group III received a combination of 0.25 and 1.25 mg kg^{-1} bupivacaine and ketamine, respectively. Injections were performed in epidural space and blood samples were obtained before injection (baseline) and 30 min thereafter. For biochemical evaluation, glucose, BUN, creatinine, TP, SGPT, Na^+ and K^+ and for hematologic evaluation, PCV, RBC, WBC and differential count of WBC, were measured. All data were analyzed by paired-samples t-test. Serum glucose level showed significant changes in all groups ($p<0.05$). Also, significant changes were observed in RBC and TP levels in group III ($p<0.05$). Other parameters did not show significant differences ($p>0.05$). It is concluded that bupivacaine and ketamine combination can be used for a safe and effective epidural analgesia in Chall sheep.

Key words: Hematochemical, epidural analgesia, bupivacaine, ketamine, sheep

INTRODUCTION

Caudal epidural analgesia can be used in performing perineum, rectum and vagina surgeries in the standing animal. Epidural analgesia is usually produced by local anesthetics (usually lidocaine 2% solution) injected into the epidural space. Ruminants are not generally considered good subjects for general anesthesia mainly because of hazards of regurgitation and inhalation of ruminal contents or saliva into the airways and lungs if the airway is left unprotected. Thus, regional anesthesia produced by the perineural or epidural injections of anesthetic agents is most frequently employed in these species. The epidural anesthetics used in farm animal practice include lidocaine, xylazine, ketamine and bupivacaine. The choice of an analgesic regimen in a particular setting is thus, a complex matter, dependent on factors such as the animal species involved, the type and duration of surgery, the severity of the pain and the efficacy of the analgesics. In an effort to approach the ideal requirements, the technique of mixing two anesthetic agents might be employed to take advantage of both agents. The effects of bupivacaine and xylazine have been compared to that of their combination in goats (Adetunji *et al*., 2002). Ketamine and xylazine have been evaluated in epidural administration with regard to clinicophysiological and hematobiochemical parameters in goats (Aithal *et al*., 1997; Singh *et al*., 2007) and sheep (Hughan *et al*., 2001). Epidural administration of ketamine in horses (Gómez de Segura *et al*., 1998) can provide sufficient analgesia without any alteration of cardiovascular and respiratory functions. Mixtures of lidocaine and bupivacaine have been used for several years to utilize the beneficial properties of both agents (Magee *et al*., 1983; Seow *et al*., 1982). In llamas, a lidocaine/xylazine mixture provided rapid onset and prolonged duration of analgesia (Grubb *et al*., 1993). Clinicophysiological and hematobiochemical effects of epidurally administered bupivacaine have been evaluated in goats (Singh *et al*., 2006).

In this study, we chose combined ketamine and bupivacaine for assessment because they act at different sites in the nociceptive pathway. The aim of this study was to compare the effects of the epidurally administered

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bupivacaine, ketamine and bupivacaine-ketamine combination on some of the biochemical and hematologic parameters in Chall sheep.

MATERIALS AND METHODS

Animals: Nine healthy male and non-gravid female Iranian Chall sheep with mean body weight of 38.89±15.12 kg and aged 12-24 months were selected randomly. They were kept for 1 week in the stable to acclimatize to the new environment. They were kept under similar conditions and feed with hay and water *ad libitum*. On the basis of clinical and hematologic evaluations, the sheep were judged to be in good health, just before the commencement of the trials. To make sure that the animals are in similar state of health, however, they were treated with oxytetracycline 5% (Oxyvet® 5%, Razak Laboratories, Iran) for 3 days at 10 mg kg^{-1}, IM, s.i.d and albendazole (Albendazole 600 mg, Iran Veterinary Drugs Production Co., Iran) at 15 mg kg^{-1}, PO, single dose.

Experimental procedure: The sheep were divided into three different groups with 3 animals in each. Three series of trials were carried out. Group I received epidural administration of 0.5% bupivacaine hydrochloride (B; Bupivacaïne MERCK®, MERCK génériques, France) alone; group II received similar administration of 5% ketamine hydrochloride (K Ketamine Hydrochloride 50 mg mL^{-1}, Rotex Medica, Germany) alone, while group III received similar administration of 0.5% bupivacaine hydrochloride plus 5% ketamine hydrochloride (BK) mixture at half their doses when used alone.

A pilot study was carried out on some of the sheep to determine the effective doses of B and K. These were found to be 0.5 and 2.5 mg kg^{-1} for B and K, respectively, hence in combination, half of their determined effective doses would be 0.25 and 1.25 mg kg^{-1} for B and K, respectively. The calculated volumes of K and BK were diluted with injectable saline solution so that they equaled that of B. The volumes used for 10 kg of body mass were 1 and 0.5 mL when injected alone and 0.5 and 0.25 mL when used together for B and K, respectively (Table 1). No color change or precipitation resulted from mixing.

Blood samples analysis: Blood samples were obtained prior to injections (baseline) and 30 min thereafter (time 30) from jugular vein and the amount of sampling was 5 mL. The blood samples of each animal were immediately transferred to test tubes; half in test tube containing anticoagulant EDTA for hematologic evaluation, half in plane test tube (VACUTAINER®, SST® Gel and Clot Activator, UK), which was then centrifuged (5×10^3 rpm for 10 min) to separate serum for biochemical evaluation. Glucose, Blood Urea Nitrogen (BUN), creatinine, total protein (TP), albumin, globulin, alanine aminotransferase (ALT or SGPT) (Singh *et al*., 2006), sodium (Na^+) and potassium (K^+) levels, for biochemical evaluation and also Packed Cell Volume (PCV), Hemoglobin (Hb), Mean Corpuscular Hb (MCH), Mean Corpuscular Hb Concentration (MCHC), Fibrinogen (Fib), Red Blood Cell count (RBC), White Blood Cell count (WBC) and differential count of WBC levels, for hematologic evaluation, were measured. Biochemical parameters were measured by an autoanalyzer (Hitachi 902, Japan) and hematologic parameters were manually measured.

Table 1: Implemented doses of drugs based on pilot study and calculated volumes of each

Drug	Dose (mg kg^{-1})	Volume (mL 10 kg^{-1})
Bupivacaine	0.5	1
Ketamine	2.5	0.5
Bupivacaine + Ketamine	0.25 + 1.25	0.5 + 0.25

Administration of drugs: For each injection, the sheep was restrained in lateral decubitus with lumbosacral spine in full flexion. Before positioning, the lumbosacral region was clipped and prepared as for surgery for performing an aseptic epidural injection. The lumbosacral site was identified and the injection was made as previously described by Hall and Clarke (1991). The site of introduction of needle was infiltrated with 1-3 mL (depending on body mass) of 2% lidocaine without epinephrine solution using a fine needle. A sterile 18 gauge 3.25 cm long hypodermic needle was inserted through the skin and directed to lumbosacral space. When the needle point was judged to have penetrated the ligamentum flavum, a 10 mL syringe containing 2 mL of air was attached to the needle. Then the needle was advanced cautiously, while exerting a concomitant pressure on the plunger until resistance to injection of the air was lost. The second syringe containing appropriate anesthetic drug was then attached to needle and administration was made slowly over 10 sec.

Statistical analysis: All the data was analyzed using paired-samples t-test with significant level at $p<0.05$ (SPSS for Windows, version 15.0, SPSS Inc).

RESULTS

Mean changes of values before and 30 min after the treatments are presented in Table 2. Glucose level increased significantly in all 3 groups ($p<0.05$). These changes are summarized in Fig. 1. RBC and TP levels significantly decreased in group III ($p<0.01$). Figure 2 and 3 illustrate changes of RBC nd TP levels.

Table 2: Changes of measured biochemical and hematologic parameters 30 min after epidural analgesia by bupivacaine (B; 0.5 mg kg^{-1}), ketamine (K; 2.5 mg kg^{-1}) and their combination (BK; 0.25 + 1.25 mg kg^{-1}) in Chall sheep

	Treatment		
Values	B	K	BK
Glucose (mg dL^{-1})	11.33±1.24*†	5.67±1.53*†	8.00±1.00*†
BUN (mg dL^{-1})	0.67±0.58‡	0.33±0.58†	0.33±0.58†
Creatinine (mg dL^{-1})	0.00±0.05	0.03±0.06‡	0.01±0.02‡
TP (g dL^{-1})	0.30±0.20‡	0.07±0.25‡	0.33±0.06**‡
Albumin (g dL^{-1})	0.13±0.12‡	0.03±0.06‡	0.20±0.10‡
Globulin (g dL^{-1})	0.17±0.23‡	0.03±0.21‡	0.13±0.12‡
SGPT (mU mL^{-1})	1.00±0.00‡	0.67±1.53†	1.67±1.15‡
Na^+ (mEq L^{-1})	2.67±2.52‡	1.67±3.51‡	0.00±2.00
K^+ (mEq L^{-1})	0.30±0.36‡	0.03±0.06‡	0.20±0.20‡
PCV (%)	1.83±1.15†	0.83±1.89‡	2.33±1.04‡
Hb (g dL^{-1})	0.67±0.29‡	0.17±0.29‡	1.00±0.50‡
MCV (fl)	0.67±1.15†	0.33±0.58‡	1.33±0.58‡
MCHC (g dL^{-1})	0.67±0.29‡	0.00±0.00	1.50±0.50‡
Fib (g dL^{-1})	0.03±0.06†	0.03±0.06†	0.03±0.06†
RBC (10^6 μg^{-1})	0.85±0.61‡	0.12±0.59‡	1.15±0.09**‡
WBC (n μg^{-1})	0.00±0.00	0.00±0.00	0.00±0.00
PMN (%)	2.00±2.00†	1.67±3.06‡	0.67±3.21†
Band Nph (%)	0.67±0.58‡	0.33±0.58†	0.00±1.00
Lym (%)	0.67±3.06‡	2.00±1.73†	0.67±2.31‡
Mon (%)	0.33±1.15†	0.33±0.58†	0.33±1.53†
Eos (%)	1.00±1.00‡	0.33±2.08‡	0.33±0.58‡
Bas (%)	0.00±0.00	0.00±0.00	0.00±0.00

*p<0.05; **p<0.01, time 30 min baseline (mean±S.D.), †Increased; ‡Decreased

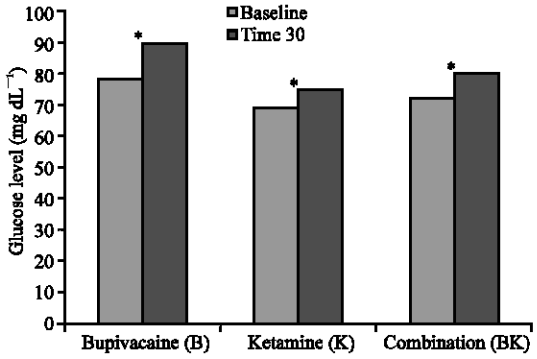

Fig. 1: Mean changes of blood glucose levels after epidural analgesia by B, K and BK in Chall sheep; *p<0.05

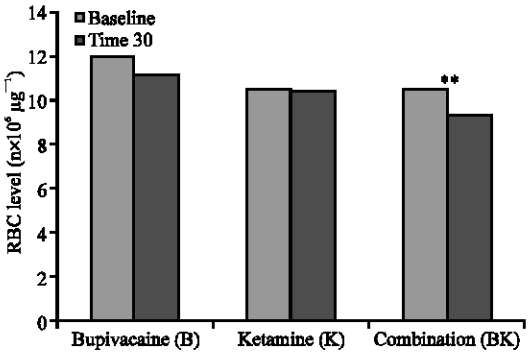

Fig. 2: Mean changes of RBC levels after epidural analgesia by B, K and BK in Chall sheep; **p<0.01

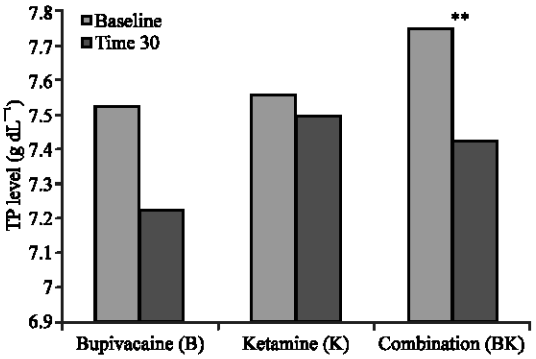

Fig. 3: Mean changes of plasma total protein levels after epidural analgesia by B, K and BK in Chall sheep; **p<0.01

The PCV increased in group I and decreased in groups II and III insignificantly, which the lowest decrease was observed in group II with the most being in group III. Although insignificant, the decrease of PCV in group III was considerable (p = 0.06). Albumin decreased in group III insignificantly. There were no significant differences in other parameters (p>0.05).

DISCUSSION

Sheep receiving the drugs in all three groups had increased plasma glucose concentration. The highest increase was in group I (B) and the lowest was in group II (K). The increase of glucose in group III (BK) was between that of group I and II. This change, increase of glucose concentration, may be due to effects of stress-induced secretion of cortisol. Restrained sheep are inevitably under stress which results in an immediate and significant increase of ACTH secretion from pituitary gland followed by dramatic rises in cortisol secretion from adrenal gland. Secreted cortisol stimulates gluconeogenesis and also reduces the consumption of glucose by cells, which both result in increased blood glucose concentration (Guyton and Hall, 2006). The lowest increase seen in group II may indicate a relatively reduced level of stress in this group; hence we can conclude that ketamine may have decreasing effects on stress. Considering group III, with regard to glucose level increase, between those two groups gives conclusive proof that ketamine does have stress relieving effects. Decreasing effects of ketamine combination on stress has been described before (Hughan *et al*., 2001; DeRossi *et al*., 2005).

Considerable amount of RBC's are reserved in spleen (Fry and McGavin, 2007). Stress via increase of catecholamine, can result in contraction of spleen and

consequently increase of PCV (Goldstein, 2003). Hence, almost all tranquilizers decrease PCV by eliminating stress. In this study, K and BK, unlike B, have been able to decrease PCV. Although, the decreases were not significant ($p>0.05$), they were so close to the significant level, especially in group III ($p = 0.06$). We may consider that K has tranquilizing effects. Logically, the most decrease must be seen in group II, but the least decrease was seen in group II.

During bleeding or taking blood samples from jugular vein, because of a decrease in circulating blood volume, intercellular fluids pass through circulation, causing PCV to decrease. Conclusively, because of the stress induced by taking blood samples and restraining, PCV increased in all groups at first, later however, after anesthesia, because of reduction of stress following the injection of the drug PCV decreased in groups II and III. In group I however, the high primary level was maintained.

Decreased amount of TP may be assigned to the inability in measuring protein which is bonded to the administered drug.

Some other hematochemical parameters which were evaluated because of their importance in anesthesia and surgical operations did not significantly change. These findings are compatible with other studies (Singh *et al*., 2007).

CONCLUSION

It is concluded that bupivacaine and ketamine combination can be used for a safe and effective epidural analgesia in Chall sheep. Since there were no significant changes in parameters like creatinine, BUN and SGPT, we can use each drug in patients with kidney and liver disorders for caudal epidural analgesia.

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REFERENCES

Adetunji, A., R.A. Ajadi and R.E. Opia, 2002. A comparison of epidural anaesthesia with xylazine, bupivacaine and bupivacaine/xylazine mixture in West African Dwarf goats. Isr. J. Vet. Med., 57: 104-109.

Aithal, H.P., Amarpal, K. Pratap and G.R. Singh, 1997. Clinical effects of epidurally administered ketamine and xylazine in goats. Small Rumin. Res., 24: 55-64.

DeRossi, R., A.L. Junqueira, R.A. Lopez and M.P. Beretta, 2005. Use of ketamine or lidocaine combination for subarachnoid analgesia in goats. Small Rumin. Res., 59: 95-101.

Fry, M.M. and M.D. McGavin, 2007. Bone Marrow, Blood Cells and Lymphatic System. In: McGavin, M.D. and J.F. Zachary (Eds.). Pathologic Basis of Veterinary Disease. 4th Edn. Missouri: Mosby Elsevier, pp: 751-755.

Goldstein, D.S., 2003. Catecholamines and stress. Endocr. Regul., 37: 69.

Gómez de Segura, I.A., R. DeRossi, M. Santos, J. SanRoman and F.J. Tendillo, 1998. Epidural injection of ketamine for perineal analgesia in horse. Vet. Surg., 27: 384-391.

Grubb, T.L., T.W. Riebold and M.S. Haber, 1993. Evaluation of lidocaine, xylazine and a combination of lidocaine and xylazine for epidural analgesia in Ilamas. J. Vet. Med. Assoc., 203: 1411-1414.

Guyton, A.C. and J.E. Hall, 2006. Adrenocortical Hormones. In: Textbook of Medical Physiology. 11th Edn. Philadelphia: Elsevier Saunders Inc., pp: 951-954.

Hall, L.W. and K.W. Clarke, 1991. Veterinary Anaesthesia. 9th Edn. Bailliere Tindall, London, pp: 263-264.

Hughan, S.C., J.M. Loose, D.J. Caddy, B.J. Canny, A.J. Tilbrook and I.R. Young, 2001. Combined xylazine and ketamine as an analgesic regimen in sheep. Aust. Vet. J., 79: 207-211.

Magee, D.A., P.T. Sweet and A.J.C. Holland, 1983. Epidural anaesthesia with mixture of bupivacaine and lidocaine. Can. Anaesth. Soc. J., 30: 174-178.

Seow, L.T., P.S. Lips and M.J. Cousins *et al*., 1982. Lidocaine and bupivacaine mixtures for epidural blockade. Anaesth., 56: 177-183.

Singh, K., P. Kinjavdekar, Amarpal, H.P. Aithal, A. Gopinathan, G.R. Sing, A.M. Pawde and K. Pratap, 2006. Comparison of analgesic, clinicophysiological and hematobiochemical effects of epidural bupivacaine in healthy and uremic goats. Small Rumin. Res., 71: 13-20.

Singh, K., P. Kinjavdekar, Amarpal, H.P. Aithal, A. Gopinathan, G.R. Sing, A.M. Pawde and K. Pratap, 2007. Effects of epidural ketamine-xylazine combination on the clinicophysiological and haematobiochemical parameters of uremic and healthy goats. Vet. Res. Commun., 31: 133-142.