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Study on the effect of epidural ropivacaine in combination with dexmedetomidine anesthesia on haemato-biochemical alteration in cattle

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Abstract
The current investigation was carried out on six cattle aged between 1-3 years to investigate haemato-biochemical alterations after receiving ropivacaine and dexmedetomidine as an epidural anaesthesia. The animals were administered with ropivacaine 0.75% at 0.25 mg/kg b.wt. and dexmedetomidine at 5 µg/kg b.wt. in sacrococcygeal space. Haematological parameter such as Haemoglobin percent (Hb%), PCV, TEC and TLC initially decreased and returned near to its baseline value at the end of observation period. Biochemical parameters such as ALT, AST, BUN and CRE increased non-significantly and a significant increase in Glucose value was observed till 90 minutes which returned to its normal base line value at 24 hours. Following epidural administration of ropivacaine combined with dexmedetomidine, temporary and compensatory alterations were seen. Ropivacaine-dexmedetomidine produces early onset of analgesia, profound analgesia, longer duration of analgesia, adequate cardio-respiratory stability and renal function with least effects on haematological and biochemical profiles.

Keywords: Cattle, dexmedetomidine, epidural anaesthesia, haemato-biochemical alterations, ropivacaine

Introduction
In standing animals, local anaesthesia during surgical procedures is preferred. Hence, in ruminant surgery, it is common to use paravertebral nerve block, local infiltration of anaesthetic agents, intravenous regional limb perfusion and epidural anaesthesia. Epidural anaesthesia has an advantage over general anaesthesia as it is well suited for aged and debilitated animal. It is well tolerated even in hypovolemic and toxic condition contrary to well known side effect of general anaesthesia. Regional anaesthesia is favoured in ruminants than general anaesthesia for surgical procedures because it is free from any hazardous side effects (Fierheller *et al*., 2004) [5]. In comparison to bupivacaine, which has all of its benefits, ropivacaine is a more recent long-acting amide local anaesthetic with a high margin of safety (Casati and putzu, 2005) [3]. According to reports, ropivacaine has a potency that is comparable to bupivacaine but four times greater than mepivacaine. Bupivacaine has been replaced by ropivacaine because it has similar analgesic effects, less motorblocks, less cardiac depressant, less neuro toxic nature, less arrhythmogenic and decreased propensity of cardio toxicity. It is less likely to penetrate large myelinated motor fibres than bupivacaine and less lipophilic, resulting in a significantly reduced motor blockade (Kamble *et al*., 2016a) [9]. Alpha-2 adrenoceptor agonist dexmedetomidine is approved for use as an intravenous sedative and co-analgesic. By blocking the release of norepinephrine, alpha-2 agonists activate the alpha-2 adrenergic receptors (alpha 2A/D, alpha 2C) in the substantia gelatinosa of the dorsal horn of the spinal cord, producing significant analgesia with hardly any sedative or cardiovascular effects (Greene *et al*., 1995) [7].

Materials and Methods
The present research was done on six adult cattle aged between 1-3 years. The animals were administered with ropivacaine 0.75% at 0.25 mg/kg b.wt. and dexmedetomidine at 5 µg/kg b.wt. in sacrococcygeal space. From each animal, 5 ml of blood were taken aseptically at 0, 30, 60, 90 minutes and 24 hours time interval after epidural analgesia for haematological and biochemical studies. Total Erythrocytes Count (TEC million/mm^3), Haemoglobin concentration (Hb in gm %), Packed cell volume (PCV %) and Total Leucocytes Counts (TLC

thousand/mm^3) were assessed as per the procedure described by Chouhan and Chandra (2007) [4]. Different biochemical parameter like blood urea nitrogen (mg/dl), blood glucose (mg/dl), serum creatinine (mg/dl), ALT and AST were estimated at 0 minute (base line) and at 30, 60, 90 minutes and 24 hours time interval after epidural analgesia by using standard kits.

Result and Discussion

A significant decrease of Hb were reported at 30 and 60 minutes in comparision to baseline value which was followed by slight increase of Hb at 90 minutes and 24 hours from 60 minutes time interval. These finding are in agreement with Mazumdar *et al*. (2015) [14] in dogs, Kamble *et al*. (2016c) [11] and Jaiswal *et al*. (2017) [8] in buffalo calves, Kumari *et al*. (2017) [13] in goats, who claimed that the value of haemoglobin decreased during the administration of ropivacaine-dexmedetomidine as an epidural anaesthesia. On contrary Gautam *et al*. (2017) [6] noticed no significant alteration in Hb values following subarachnoid administration of ropivacaine, dexmedetomidine and its combination in buffalos. In the current study, the sequestration of blood cells in the spleen, which led to a reduction in the total number of erythrocytes in circulation and a concurrent decrease in the Hb value (Jaiswal *et al*. 2016) [8] which is induced by the medication that blocks alpha-2 adrenoceptors' adrenolytic effects (Kumar *et al*., 2016) [12]. A non-significant increase of PCV was reported at 30 minutes in comparison to baseline value, which was followed by non-significant decrease at 60 and 90 minutes. Thereafter, a significant decrease was noticed at 24 hrs in comparison to 90 minutes time interval. These finding are in agreement with Mazumdar *et al.* (2015) [14] in dogs, Kamble *et al*. (2016c) [11] in buffalo calves, Jaiswal *et al*. (2017) [8] in buffalo calves, Kumari *et al*. (2017) [13] in goats, Saini *et al.* (2019) [16] in dogs and Poonia *et al.* (2022) [15] in dogs, who noticed non-significant decrease in PCV following ropivacaine and dexmedetomidine analgesia. Similarly, Bisht *et al*. (2016) [2] reported significant decrease in PCV following dexmedetomidine administration in dogs. These findings are on contrary with Gautam *et al*. (2017) [6] in buffaloes and Barot *et al.* (2022) [1] in bovines, who observed no significant change in PCV following dexmedetomidine analgesia. In the current study, the decrease in PCV could be explained by the sequestration of blood cells in the spleen, which causes a simultaneous decrease in the PCV and total erythrocyte count in circulation (Jaiswal *et al*., 2016) [8] induced by the adrenolytic property of alpha-2 adrenoceptor drug (Kumar *et al*., 2016) [12]. A non-significant decrease of TEC value were reported at 30 and 60 minutes in comparison to baseline value. Thereafter, a slight increase was noticed at 90 minutes as compared to 60 minutes time interval. The value of TEC reached near to its baseline value at 24 hours time interval. These finding are in agreement with Saini *et al*. (2019) [16] in dogs, Poonia *et al*. (2022) [15] in dogs, who noticed non-significant reduction in TEC value following administration of dexmedetomidine and its combination. On contrary to these findings Kumari *et al*. (2017) [13] in goats, reported no significant difference in TEC value following epidural administration of ropivacaine-dexmedetomidine. The pooling of blood cells in the spleen caused by the adrenolytic properties of alpha-2 adrenoceptor drugs and dissociative anaesthetic agents could be the cause of the decrease in TEC at various time intervals (Saini *et al*. 2019) [16]. A significant decrease of TLC value were reported at 30 minutes in comparision to baseline value. Thereafter, a progressive increase was noticed from 60 minutes to 24 hrs as compared to 30 minutes time interval. These finding are in agreement with Kumari *et al*. (2017) [13] in goats, Saini *et al*. (2019) [16] in dogs, who reported increase in TLC value following administration of ropivacaine, dexmedetomidine and its combination anaesthesia. Similarly, Poonia *et al*. (2022) [15] reported decrease of TLC value following administration of dexmedetomidine/midazolam-ketamine anaesthesia in dogs. These above finding are on contrary with Gautam *et al*. (2017) [6], who noticed no significant difference in TLC value following subarachnoid administration of ropivacaine, dexmedetomidine and its combination with ketamine in urolithic buffalos. This increase in TLC value may be attributed to stress and release of ACTH because of their administration. The increase in plasma volume due to vascular pooling after anaesthesia administration or confinement of RBC in the spleen and lung could also contribute to the decrease in TLC value by increasing adrenaline or nor-adrenaline concentration in peripheral circulation, which inhibits leukocyte proliferative activity (Venugopal *et al*., 2002) [19]. A non-significant increase in the value of ALT was reported from 30 to 90 minutes as compared to baseline value and reached toward its baseline value at 24 hrs time interval. Similar finding were noticed by Kumar *et al.* (2016) [12] in dogs, Kamble *et al.* (2016b) [10] in buffalo calves, Kumari *et al*. (2017) [13] in goats, Saini *et al*. (2019) [16] in dogs, Sekhar *et al*. (2020) [17] in cattle, who observed non-significant increase in the value of ALT following ropivacaine and dexmedetomidine analgesia. The complete biotransformation of ropivacaine and dexmedetomidine into inactive metabolites in the liver, mediated by cytochrome P450 and aliphatic hydroxylation, might be responsible for the increase in ALT values (Kumari *et al*. 2017) [13]. A non-significant increase in value of AST was reported from 30 to 90 minutes time interval in comparison to baseline value and reached near to its baseline value at 24 hour time interval. These finding are in agreement with Kumar *et al*. (2016) [12] in dogs, Kamble *et al*. (2016b) [10] in buffalo calves, Kumari *et al*. (2017) [13] in goats, Saini *et al*. (2019) [16] in dogs, Sekhar *et al*. (2020) [17], who observed non-significant increase in the value of ALT following ropivacaine and dexmedetomidine analgesia. The entire biotransformation of ropivacaine and dexmedetomidine via glucoronidation and aliphatic hydroxylation to inactive metabolites occurs in the liver and may account for the rise in AST values (Kumari *et al*. 2017) [13]. A significant increase in the value of blood glucose was reported from 30 minutes to 90 minutes in comparison to baseline value. Thereafter, a significant decrease noticed at 24 hours time interval as compared to 90 minutes time interval, which reached near its baseline value. Similar findings were too reported by Mazumdar *et al*. (2015) [14] in dogs, Kamble *et al.* (2016b) [10] in buffalo calves, Jaiswal *et al*. (2017) [8] in buffalo calves, Kumari *et al*. (2017) [13] in goats, Gautam *et al*. (2017) [6] in buffalos and Sekhar *et al*. (2022) [17] in cattles, who observed significant increase in the value of glucose after ropivacaine and dexmedetomidine analgesia. These findings are in partial agreement with Saini *et al*. (2019) [16] who noticed non-significant rise in glucose value following administration of dexmedetomidine and its combination in dogs. The increase in glucose value may be caused by CNS depression, animal stress that stimulates pancreatic B cells to block insulin release, and an increase in liver glucose synthesis (Kumari *et*

al. 2017) [13]. A significant increase in the value of BUN was reported from 30 minutes to 90 minutes in comparison to baseline value and reached towards its baseline value at 24 hours time interval. These findings corroborates with Kamble *et al*. (2016b), Jaiswal *et al*. (2017) [8] in buffalo calves, who noticed a significant increase in the value of BUN following epidural administration of ropivacaine-dexmedetomidine and dexmedetomidine. Similar finding were also observed by Saini *et al*. (2019) [16], who reported significant increase in the value of BUN following intravenous injection of dexmedetomidine and thiopental sodium in dogs. These findings partially concur with Saini *et al*. (2019) [16], who reported a non-significant increase in the value of BUN after intravenous injection of dexmedetomidine and ketamine in dogs. The increase in the value of blood urea nitrogen might be due to temporary reduction in blood flow to kidneys (Umar and Adam., 2013) [18]. It might be caused by the short-term inhibition of renal blood flow by an alpha-2 agonist, which leads to a reduction in glomerular filtration rate and an increase in blood urea nitrogen levels. A non-significant increase in the value of serum creatinine was reported at 30 minutes and followed by a significant increase from 60 minutes to 24 hours time interval in comparison to baseline value. Similar finding were reported by Kamble *et al*. (2016b) [10] in buffalo calves, Jaiswal *et al*. (2017) [8] in buffalo calves, who noticed significant increase in creatinine value following epidural injection of ropivacaine and dexmedetomidine. Bisht *et al*. (2016) [2] substantial increase in creatinine levels after dexmedetomidine anaesthesia in dogs was recorded. These findings are also in agreement with Saini *et al*. (2019) [16] in dogs, who observed significant increase in creatinine after intravenous administration of dexmedetomidine and thiopentone sodium. A temporary decrease in blood supply to the kidneys might be the cause of the elevated serum creatinine levels (Umar and Adam., 2013) [18]. It could be because alpha-2 agonists have a brief inhibitory effect on renal blood flow, which leads to a decrease in glomerular filtration rate and a rise in creatinine level.

Table 1: Effect of epidural ropivacaine in combination with dexmedetomidine anaesthesia on haematological alteration in cattle

Time	Hb(g/dl)	PCV (%)	TEC (million/µl)	TLC (thousand/µl)
0 minutes	$9.15^{a}\pm0.43$	$28.88^{abc}\pm0.27$	$5.56^{a}\pm0.29$	$12.15^{a}\pm1.21$
30 minutes	$9.03^{bc}\pm0.52$	$29.30^{ab}\pm0.26$	$5.46^{a}\pm0.12$	$7.68^{e}\pm0.16$
60 minutes	$8.90^{c}\pm0.54$	$28.53^{b}\pm0.22$	$4.50^{a}\pm0.17$	$8.37^{d}\pm0.97$
90 minutes	$8.96^{bc}\pm0.62$	$28.75^{b}\pm0.23$	$5.28^{a}\pm0.46$	$9.79^{c}\pm0.81$
24 hours	$9.10^{ab}\pm0.70$	$27.08^{c}\pm0.29$	$5.66^{a}\pm0.26$	$11.65^{b}\pm0.97$

-Mean within a column with different lower-case superscripts (a, b, c…) differ significantly between time intervals ($p\leq0.05$)

Table 2: Effect of epidural ropivacaine in combination with dexmedetomidine anaesthesia on biochemical alteration in cattle

Time	ALT (IU/L)	AST (IU/L)	Blood Glucose (mg/dl)	BUN (mg/dl)	Serum Creatinine (mg/dl)
0 minutes	$32.12^{a}\pm0.52$	$78.83^{b}\pm1.60$	$60.63^{c}\pm2.68$	$27.25^{d}\pm0.08$	$1.42^{c}\pm 0.09$
30 minutes	$34.05^{a}\pm0.47$	$83.21^{b}\pm0.77$	$95.56^{b}\pm2.53$	$30.96^{c}\pm0.20$	$1.46^{c}\pm0.13$
60 minutes	$35.75^{a}\pm0.56$	$96.66^{b}\pm1.45$	$96.55^{b}\pm2.53$	$32.16^{b}\pm0.28$	$1.56^{b}\pm0.17$
90 minutes	$36.26^{a}\pm0.61$	$98.16^{ab}\pm1.19$	$103.26^{a}\pm3.30$	$33.33^{a}\pm0.34$	$1.66^{a}\pm0.16$
24 hours	$33.34^{a}\pm0.26$	$80.00^{ab}\pm1.46$	$60.76^{c}\pm2.72$	$27.83^{d}\pm0.08$	$1.69^{a}\pm0.20$

-Mean within a column with different lower-case superscripts (a, b, c…) differ significantly between time intervals ($p\leq0.05$)

Conclusion

From the above discussion, it was concluded that ropivacaine-dexmedetomidine combination produces haepato-renal function stability with least effects on haematological and biochemical profiles. For longer duration of surgery, ropivacaine-dexmedetomidine could be recommended because all haematological and biochemical parameters returned to its base line value indicating slightest effect on vital organs.

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