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HAEMATO - BIOCHEMICAL CHANGES AFTER INTRAVENOUS ADMINISTRATION OF DEXMEDETOMIDINE COMBINED WITH BUTORPHANOL AND PENTAZOCINE FOR STANDING SEDATION IN CATTLE

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Abstract: The study was conducted to evaluate efficacy of combination dexmedetomidine - butorphanol and dexmedetomidine - pentazocine as sedative for standing sedation in cattle. The study was conducted on 16 clinical cases of animals divided in 2 groups viz., I and II with 8 animals in each group. Group I animals were sedated with dexmedetomidine (1 µg/kg b.w. IV) and butorphanol (0.05 mg/kg b.w. IV) and group II animals were sedated with dexmedetomidine (1 µg/kg b.w. IV) and pentazocine (0.05 mg/kg b.w. IV) and they were subjected for different surgeries such as amputation of horn and extirpation of eye ball under standing sedation with local analgesia. Haematological observations revealed that haemoglobin value in group I decreased significantly ($P \leq 0.01$) during sedation where as non-significant decrease in haemoglobin during sedation was noticed in group II. Packed cell volume decreased more significantly ($P \leq 0.01$) in group I when compared to group II during and after sedation. The total leucocyte count in group II decreased significantly ($P \leq 0.01$) during and after sedation. The total erythrocyte count in animals of both the groups decreased significantly ($P \leq 0.01$) during sedation. Biochemical observations revealed significant ($P \leq 0.01$) increase in blood glucose values above the normal physiological limits in all the animals of both the groups during sedation and decreased to normal value after 24 hours. No significant change was observed in alanine transaminase, aspartate transaminase and blood urea nitrogen values in both the groups after administration of the drugs. Combination of dexmedetomidine (1 µg/kg IV) and butorphanol (0.05 mg/kg IV) proved to better sedative agent in respect to haemato- biochemical changes than combination dexmedetomidine (1 µg/kg IV) and pentazocine (0.5 mg/kg IV) in cattle for standing sedation.

Keywords: Standing sedation, cattle, dexmedetomidine, butorphanol and pentazocine.

INTRODUCTION

Neuroleptanalgesia refers to the combination of tranquillisers, sedatives and opioids produces far better sedation than any of these drugs used alone as a result of synergism, and the dose of each individual agent is reduced (Joubert, 1999). Sedatives used for calming ruminants includes α_2 - adrenoceptor agonist like xylazine, detomidine, romifidine, medetomidine, phenothiazine like acepromazine, triflupromazine and opioids like butorphanol and

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pentazocine. Xylazine was first α_2- agonist to be licensed in veterinary medicine. Later in 2002 dexmedetomidine is introduced in veterinary practice which is more potent with least side effects as compare to rest of α_2 – agonists. Dexmedetomidine is a dextrorotary enantiomer of medetomidine has replaced medetomidine and other α_2 – agonists in veterinary market. It has beneficial pharmacological profile with short half life and rapid redistributation it reduces the dose requirement of opioids and anaesthetics agent and attenuates the haemodynamic responses to surgical stimuli has been studied in small ruminants (Kumar *et al*. 2014). Dexmedetomidine have shown to decrease the tubular secretion of vasopressin and to antagonize its effects on renal tubules. The sedation induced by dexmedetomidine was evaluated in various studies but the ability of the cow to remain standing during sedation with dexmedetomidine combined with opioids such as butorphanol and pentazocine was not yet reported.

Butorphanol tartrate 17-cyclobutylmethyl-morphine-3, 1-diol is a mixed opioids agonist/antagonist that provides good analgesia and mild sedation. Synergistic interaction has been reported between α_2- agonist and opioids in earlier studies (Monsang 2011). Butorphanol have analgesic properties in ruminants, however, it can also induce excitatory behavioral changes (Dzikti *et al*, 2009). It is used alone and in combination with α_2 agonist. Pentazocine is an agonist at K- receptors and produce analgesia. Unlike other opioids, pentazocine does not cause bradycardia. High dose of Pentazocine increase heart rate and blood pressure. Its analgesic potency is approximately one half that of morphine but it is five times more potent than meperidine.

An advantage of combining a sedative and an analgesic is that the combination allows the dose of either drug to be reduced while maintaining their desirable pharmacologic effects, thus preventing possible sternal recumbency with minimum hemato - biochemical changes induced by administering high doses of a sedative alone. These drug combinations, particularly dexmedetomidine with butorphanol and pentazocine, have not yet gained popularity for use in bovine practice. The purpose of this study, therefore, is to evaluate and compare the standing sedation effects on haemato – biochemical parameters induced by administering combinations of dexmedetomidine - butorphanol and dexmedetomidine - pentazocine in bovine practice.

MATERIALS AND METHODS

Animals and Treatments

Study was conducted on 16 clinical cases of cattle presented at the Teaching Veterinary Clinical Complex of College of Veterinary and Animal Sciences, Parbhani which were randomly divided into two groups viz. Group I and Group II. Each group consisted of eight animals. In all cases, fasting for 24 hrs and withhold of water for 12 hrs was followed before administration of sedative drugs. The animals of group I were administered inj. dexmedetomidine hydrochloride (1 µg/kg IV) with inj. butorphanol tartarate (0.05 mg/kg IV) and animals of group II were given dexmedetomidine hydrochloride (1 µg/kg IV) with inj. pentazocine (0.5 mg/kg IV).

Haematological estimation

For haematological and biochemical estimation the blood samples were collected preoperatively, perioperatively and postoperatively after 24 hours. Haemoglobin concentration was determined by Sahli's haemoglobinometer and expressed as gm percentage (%). Packed cell volume was determined by Wintrobe method and centrifugation at 3000 rpm and expressed as percentage (%). Total leucocyte count (TLC) was carried out by haemocytometer and expressed in thousand per cumm. Total erythrocyte count (TEC) was carried out by Neubaur's chamber and expressed in million per cumm.

Biochemical estimation

The blood glucose levels were estimated by using enzymatic GOD-Pod with commercial kit and values were expressed in mg/dl. Alanine transaminase and Aspartate transaminase was estimated by using clinical analyser with commercial kit and values were expressed as IU/L. Blood urea nitrogen was estimated by using clinical analyser with commercial kit and values were expressed as mg/dl. The data collected in the present study were analysed using conventional tools for data analysis (ANOVA and t- test). WASP 2.0 statistical package was used for the data analysis (Jangam and Wadekar, 2018).

RESULTS

Animals

The surgeries carried out under standing position in group I were amputation of horn in 5 animals and extirpation of eye ball in 3 animals correspondingly amputation of horn in 4 animals and extirpation of eye ball in 4 animals in group II, respectively.

Haematological observations

Haemoglobin

Haemoglobin (gm%) values fluctuated within normal physiological limits in animals of both the groups. The haemoglobin value in group I (dexmedetomidine @ 1 µg/kg IV and

butorphanol @ 0.05 mg/kg IV) decreased significantly (P≤0.01) during sedation where as non-significant decrease in haemoglobin during sedation was noticed in group II (dexmedetomidine @ 1 µg/kg IV and pentazocine @ 0.5 mg/kg IV). In both the groups Hb values shown non significant increase after 24 hours. The comparison between the groups at different intervals revealed no significant difference in the mean haemoglobin value.

Packed cell volume

Packed cell volume (%) fluctuated within normal physiological limits in both the groups. In both the groups I and II the packed cell volume decreased significantly (P≤0.01) during and after sedation. The packed cell volume decreased more significantly (P≤0.01) in group I (dexmedetomidine@ 1 µg/kg IV and butorphanol @ 0.05 mg/kg IV) when compared to group II (dexmedetomidine@ 1 µg/kg IV and pentazocine @ 0.5 mg/kg IV) during and after sedation.

Total leucocyte count

Total leucocyte count ($x10^3/\mu l$) fluctuated within normal physiological limits in both the groups. The total leucocyte count in group II decreased significantly (P≤0.01) during and after sedation. The comparison between the groups at different intervals revealed statistical significant (P≤0.01) difference in the total leucocyte count.

Total erythrocyte count

Total erythrocyte count ($x10^6/\mu l$) fluctuated within normal physiological limits in both the groups. The total erythrocyte count in animals of both the groups decreased significantly (P≤0.01) during sedation. The comparison between the groups at different intervals revealed significant difference (P≤0.01) after sedation in the total erythrocyte count (Depicted in Table 1).

Table1. Mean ± S.E values of Haematological parameters in animals of group I and II

Group I	Haemoglobin (gm%)	Packed cell volume (%)	Total leucocyte count ($x10^3/\mu l$)	Total erythrocyte count ($x10^6/\mu l$)
Before sedation	$^{a}12.43 \pm 0.73^{m}$	$^{a}36.75 \pm 2.35$	5.67 ± 0.80^{m}	$^{a}9.83 \pm 0.72^{m}$
During sedation	$^{b}9.33 \pm 0.69$	$^{b}28.25 \pm 1.27$	5.09 ± 0.78^{m}	$^{b}7.82 \pm 0.86$
After sedation	$^{b}9.98 \pm 0.59$	$^{b}24.75 \pm 1.06$	4.81 ± 0.65^{m}	$^{b}7.96 \pm 0.77^{m}$
Group II				
Before sedation	$^{a}10.05 \pm 0.52^{n}$	$^{a}36.00 \pm 3.61$	$^{a}8.49 \pm 0.71^{n}$	$^{a}7.46 \pm 0.65^{n}$
During sedation	$^{b}8.63 \pm 0.65$	$^{b}27.25 \pm 2.72$	$^{b}7.26 \pm 0.57^{n}$	7.58 ± 0.58
After sedation	8.65 ± 0.65	$^{b}26.25 \pm 2.20$	$^{b}6.36 \pm 0.58^{n}$	$^{b}7.37 \pm 0.66^{n}$

[a, b superscript shows significant difference at regular interval during course of sedation in a specific group only (within column) m,n superscript shows significant difference between two groups at specific interval only (within row)].

Biochemical observations

Blood glucose

The blood glucose values fluctuated above the normal physiological limits in all the animals of both the groups. In both the groups the blood glucose values increased significantly ($P \leq 0.01$) during sedation however, the values were reduced after 24 hrs. The comparison between the groups revealed significant difference ($P \leq 0.01$) during sedation and after sedation intervals.

Alanine Transaminase (ALT)

The alanine transaminase values fluctuated within normal physiological limits in both the groups. There was no significant difference between and within the groups at all the intervals of the study. The levels were within normal physiological limits in animals of both the groups.

Aspartate transaminase (AST)

The aspartate transaminase values fluctuated within normal physiological limits in both the groups. There was no significant difference between and within the groups at all the intervals of the study. The levels were within normal physiological limits in both the groups.

Blood Urea Nitrogen (BUN)

The blood urea nitrogen values fluctuated within normal physiological limits in animals of both the groups. There was no significant difference within the group I at all the intervals of the study. This indicates that renal functions are not significantly altered in dexmedetomidine@ 1 µg/kg IV and butorphanol @ 0.05 mg/kg IV sedative agents. In group II administered with dexmedetomidine@ 1 µg/kg IV and pentazocine @ 0.5 mg/kg IV the blood urea nitrogen increased significantly ($P \leq 0.01$) during sedation. The comparison between the groups revealed significant difference ($P \leq 0.01$) at all the intervals (Depicted in Table 2).

Table 2. Mean ± S.E values of Biochemical parameters in animals of group I and II

Group I	Blood glucose (mg/dl)	Alanine transaminase (IU/L)	Aspartate transaminase (IU/L)	Blood Urea Nitrogen (mg/dl)
Before sedation	$^{a}55.60 \pm 6.64$	15.62 ± 2.08	66.66 ± 5.12	16.47 ± 1.31^{m}

During sedation	$^{b}110.73 \pm 5.84^{m}$	16.68 ± 1.50	66.30 ± 5.04	19.03 ± 1.71^{m}
After sedation	$^{b}38.09 \pm 5.40^{m}$	15.59 ± 1.01	65.60 ± 4.68	18.16 ± 1.56^{m}
Group II				
Before sedation	$^{a}62.54 \pm 5.90$	16.65 ± 2.45	76.10 ± 4.93	$^{a}21.45 \pm 1.91^{n}$
During sedation	$^{b}128.52 \pm 14.54^{n}$	17.85 ± 2.53	76.00 ± 5.00	$^{b}26.08 \pm 4.28^{n}$
After sedation	59.28 ± 5.38^{n}	16.47 ± 2.35	75.81 ± 5.38	21.79 ± 0.08^{n}

[a, b superscript shows significant difference at regular interval during course of sedation in a specific group only (within column) m,n superscript shows significant difference between two groups at specific interval only (within row)]

DISCUSSION

In the present study the decrease in haemoglobin values during sedation in both the groups might be due to pooling effect of circulatory blood cells in the spleen or other reservoirs secondary to decreased sympathetic activities (Wagner *et al.,* 1991). Similar findings were reported by Monsang (2011) who observed decrease in haemoglobin after administration of dexmedetomidine @ 15 µg/kg IV in sheep. Khattri *et al.* (2013) reported significant decrease in haemoglobin after administration of dexmedetomidine hydrochloride @ 2.5 µg/kg IV anaesthesia in buffalo calves. Doiphode (2001) cattle, Jadhav (2001) observed slightly decrease in haemoglobin concentration, in cattle after administration with xylazine @ 0.1 mg/kg IV and pentazocine @ 0.5 mg/kg IV in goats.

The decrease in packed cell volume might be due to the stress caused by the sedative drugs, decreased heart rate and blood pressure. Khattri *et al.* (2013), Singh *et al.* (2013) reported significant decrease in packed cell volume after administration of dexmedetomidine hydrochloride @ 2.5 µg/kg IV in buffaloes. Doiphode (2001) cattle, Jadhav (2001) observed slightly decrease in packed cell volume, in cattle after administration with xylazine @ 0.1 mg/kg IV and pentazocine @ 0.5 mg/kg IV in goats.

Decrease in TLC might be due to adrenocortical stimulation and subsequent effects of gulcocorticoids on circulating neutrophils and lymphocytes (Shrama *et al.*, 2015). Doiphode (2001) who observed non significant decrease in total leucocyte count after administration of xylazine @ 0.1 mg/kg IV and pentazocine @ 0.5 mg/kg IV in cattle. Jadhav (2001) reported non significant decrease in total leucocyte count after administration with xylazine @ 0.1 mg/kg IV – pentazocine @ 0.5 mg/kg IV in goats. Monsang (2011) reported significant decrease in total leucocyte count after administration of dexmedetomidine @ 15 µg/kg IV in sheep.

In the present study, the decrease in total erythrocyte count might be attributed to the sedation of alpha2-agonists. Similar findings of decrease in TEC after injecting dexmedetomidine @ 15 µg/kg IV were noticed in sheep (Monsang, 2011) and cattle (Doiphode, 2001). Jadhav (2001) observed non significant decrease in total erythrocyte count, in goats after administration with xylazine @ 0.1 mg/kg IV and pentazocine @ 0.5 mg/kg IV. Kadam (2012) reported non significant change in total erythrocyte count in animals administered with xylazine @ 0.1 mg/kg IV and butorphanol @ 0.1 mg/kg IV.

The increase in blood glucose level observed during the present study might be attributed to an alpha2-adrenergic inhibition of insulin released from beta cells of pancreas and increased glucose production in the liver (Gasthuys et al., 1987). In accordance with the present findings Kumar *et al.* (2014) observed non-significant change in blood glucose values during anaesthesia after administration of dexmedetomidine hydrochloride @ 2.5 µg/kg IV with propofol 1% in uraemic goats. Doiphode (2001) reported significant rise in blood glucose in cattle after administration combination of xylazine @ 0.1 mg/kg IV and pentazocine @ 0.5 mg/kg IV.

Kadam (2012) who reported non significant change in alanine transaminase in cattle after administration of xylazine @ 0.1 mg/kg IVandbutorphanol @ 0.1 mg/kg IV. Doiphode (2001) also reported non significant change in alanine transaminase in cattle after administration with xylazine @ 0.1 mg/kg IV and pentazocine @ 0.5 mg/kg IV.

Similar findings were observed by Doiphode (2001) who reported non significant change in aspartate transaminase in cattle after administration with xylazine @ 0.1 mg/kg IV and pentazocine @ 0.5 mg/kg IV. Kadam (2012) observed non significant change in aspartate transaminase in cattle after administration with xylazine @ 0.1 mg/kg IV and butorphanol @ 0.1 mg/kg IV.

The increase in blood urea nitrogen values might be attributed to the temporary inhibitory effects of anaesthetics drugs on the renal blood flow, which in turn might have caused rise in blood urea nitrogen level as suggested by (Kinjavdekar *et al.,* 2000). Doiphode (2001) who reported non significant rise in blood urea nitrogen in cattle after administration with pentazocine @ 0.5 mg/kg IV. Khattri *et al.* (2013) reported a significant increase in urea nitrogen from 15 to 60 minutes after administration of dexmedetomidine @ 2.5 µg/kg IV and propofol 1%, which might be due to temporary inhibitory effects of anaesthetic drugs on the renal blood flow. Kumar *et al.* (2013) observed non-significant change in plasma urea nitrogen in uraemic goats administered with dexmedetomidine @ 2.5 µg/kg IV – propofol

1%. Kadam (2012) reported non significant decrease in blood urea nitrogen in cattle administered with xylazine @ 0.1 mg/kg IV and butorphanol @ 0.1 mg/kg IV.

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