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Comparative evaluation of romifidine-ketamine and xylazine-ketamine induction combination for isoflurane anaesthesia in cattle

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Abstract
The study was conducted in 12 clinical cases presented to TVCC, Bidar. Twelve animals were randomly divided in to two groups viz., Group-I and Group-II consisting of six animals in each group. Group –I animals received Romifidine (10µg/kg) intravenously, 10minutes later ketamine was given @3mg/kg body weight intravenously for induction of anaesthesia. In Group-II animal's xylazine (0.1mg/kg) was administered intravenously, 10minutes later ketamine was given @3mg/kg body weight intravenously for induction of anaesthesia followed by immediate intubation, maintaenance of anaesthesia was done under isoflurane in both the groups. Anaesthetic combinations were compared by clinic physiological, haemodynamic and haematological observations. The induction and recovery were smooth and uneventful in both the groups. Induction was quicker in group-I animals. Physiological and haemodynamic parameters like heart rate, respiratory rate, rectal temperature, mean arterial pressure and haemoglobin oxygen saturation were fluctuated within normal limit.non significant bradycardia in group-I. Intermittent apnoea was observed in all animals, frequency was higher in group-I. heamoglobin packed cell volume and total erythrocyte count were decreased non-significantly in both the groups. Nuetrophilia and relative lymphocytopenia was recorded in both the groups. In conclusion romifidine as pre-anaesthetic for ketamine and isoflurane anaesthetic maintenance is a better combination than xylazine – ketamine and isoflurane anaesthetic mainatnanace in cattle.

Keywords: cattle, romifidine, xylazine, isoflurane

Introduction
Cattle usually accept physical restraint well and that to in conjuction with local or regional anaesthesia is often sufficient for completion of many surgical procedures. However, many times in non-co-operative animals and in diagnostic and surgical procedure that are more complex like, diaphragmatic hernia, traumatic pericardities and orthopedic surgeries where technical and anatomical aspects of the surgical procedures warrant absolute control of movement during surgery (Kumar *et al.,* 2013) [15]. General anaesthesia in cattle involves complexities like, regurgitation bloat, respiratory complication and nerve paralysis which are not often encountered in small animals, however, carefully selected and properly managed general anaesthetic techniques provide optimal condition for surgery. Xylazine is an alpha2-adrenergic agonist drug used to induce tranquilization and or sedation which provides good muscle relaxation and analgesia during surgery, however, it carries the risk of suppressing the cardio-vascular system (England and Clarke, 1996) [7]. Currently ketamine is used as induction agent in cattle, along with several pre-anaesthetic agent, xylazine (Aria *et al.,* 2006) [4], diazepam (Riazuddin *et al.,* 2004a), accepromazine (Kumar *et al.,* 2012) [14] and Guaifenesin (Riazoddin *et al*., 2004b) [22] under isoflurane anaesthesia. However, there is paucity of reports on studies of romifidine-ketamine induction and isoflurane maintenance. Hence the present study was under
taken to evaluate the feasibility of Romifidine–Ketamine induction and Isoflurane maintenance anaesthesia in cattle subjected to various clinical surgeries.

Materials and Method
The study was conducted in 12 clinical cases presented to TVCC, Veterinary College, Bidar with various surgical conditions. Twelve clinical cases were randomly divided in two groups *viz.,* group-I and group-II with six animals in each group, the group-I animals were given romifidine[1] HCl @10µg/kg body weight intravenously. 10 minutes later Ketamine[2] HCl was given @3mg/kg body weight intravenously for the induction of anaesthesia followed by

immediate intubation, the animals were maintained on 5 per cent to 1 per cent of isoflurane. Group-II animals were given xylazine[3] HCl @0.1mg/kg body weight intravenously. 10minutes later Ketamine HCl was given @3mg/kg body weight intravenously for the induction of anaesthesia followed by immediate intubation, the animal were maintained on 5 per cent to 1.5 per cent. The details of the cases and operation performed are given in table no: 1.

The Physiological parameters *viz.,* rectal temperature, respiratory rate, heart rate and hemodynamic parameters *viz.,* hemoglobin level, packed cell value, total erythrocytes count (TEC), total leucocytes count (TLC), differential leucocytes count (DLC) were estimated at 0, 10, 5, 15, 30, 60 and 120 minutes after ketamine administration.

Results and Discussion

I. Physiological Parameters

The Mean ± SE values of physiological parameters are given in table no.1 and Fig.1

Rectal Temperature (ºF)

In group-I, the Mean ± SE values of rectal temperature significantly decreased was observed at 5 minutes after administration of Romifidine and ketamine when compared to before administration of anaesthesia. The trend of decrease in value was observed up to 60 minutes of anaesthesia, and at 120 minutes, it returned to near normal physiological limit. However the fluctuation in temperature was within the physiological limit. In group-II, the significant drop in temperature was observed at 30 minutes after administration of xylazine and ketamine anaesthesia and return to normal at 120 minutes after anaesthesia. When compared between the group, no significant difference was observed, however, at 0 minutes group-I animals had significantly higher rectal temperature ($p \leq 0.05$) than group-II animals, however the values of rectal temperature of both group were within physiological limit.

The decrease in rectal temperature in present study could be due to the reduced muscle tone, reduction of metabolic rate and CNS depression by anaesthetic agent (Lu *et al.,* 2013) [12] and depression of thermo-regulatory centre. A significant decrease in rectal was reported by Singh *et al.,* (2012) [17].

Respiratory Rate (breaths/min)

In group-I, the Mean ± SE values of respiratory rate decreased significantly ($p \leq 0.05$) after 10 minutes of Romifidine administration, there after it showed increase trend which was statistically significant ($p \leq 0.05$) only at 120 minutes after ketamine administration. Similar trend was observed in group-II animals. Comparison between the groups showed non-significant variation at all the interval of schedule.

There was non-significant difference was observed between the groups. The respiratory rate was significantly decreased up to 10 minutes after romifidine induction as well as xylazine induction in both the group. The Bradypnoea statistically significant at 10 minutes ($p \leq 0.05$), it could be due to depression of CNS by xylazine or romifidne (Amresh kumar *et al.,* 1979) [3] and due to activation of α-2-adrenergic pathway, leading to inhibition of local coeruleus neurons (Guo *et al.,* 1996) [8], similar findings were recorded by Demirkhan *et al.,* (2002).

Heart Rate (beats/min)

In group-I animals bradycardia was observed from 10 minutes to 60 minutes after romifidine, ketamine and isoflurane administration, however, the heart rate was returned to normal at 120 minutes after anaesthesia**.** Similar trend was observed in group-II animals. Comparison between the groups showed non-significant variation at all interval of schedule.

Bradycardia was observed from 10 minutes to 60 minutes of anaesthetic intervals in both the group of animals, however the bradycardia was statistically non-significant from 10 minutes to 60 minutes of interval in both groups. It could be due to reflex bradycardia as a result of α-2 agonist induced vasoconstriction (Lemke, 2007) [11], the results in agreements with earlier study by Haskins *et al.* (1985) [10] in dogs and by Stegmann (1998) [26] and Abu-Ahmad (2013) [1] in goats.

II. Heamodynamics

Mean Arterial Pressure (mm of Hg)

In group-I, the Mean±SE values of mean artial pressure was calculated and there was no significant changes were observed. In group-II, the Mean±SE values of mean artial pressure was calculated and at 5 minutes after xylazine-ketamine anaesthesia there decrease was observed followed by increase in the mean arterial pressure at 15 minutes, 30, 60 and 120 minutes after anaesthesia and the increase was under physiological limit. Comparison between the groups revealed that, the mean arterial pressure was significantly higher ($p \leq 0.05$) at 5 minutes after ketamine administration than group-II animals.

Mean arterial pressure (MAP) fluctuated within the physiological limit throughout anaesthetic interval, however in group-II animals at 5 minutes after xylazine-ketamine administration, decrease in mean arterial pressure was observed which might be due to central vegal effect on heart and direct action on vasculature (Peshin *et al.,* 1980) [20] and Bamiadam *et al.* (2007) reported significant decrease in the mean arterial pressure in sheep.

Although all the pre-anaesthetic and Isoflurane used had depressant effect on MAP as reported by earlier workers (Steffey and Mamma, 1977; Perry *et al.,* 1982 and Nain *et al.,* 2010) [25, 17].

Haemoglobin Oxygen Saturation (SPO_2) (%)

Group-I, the Mean±SE values of mean artial pressure were calculated and there was non-significant difference was observed within the group at different interval. Similar trend was observed in group-II animals. When compared between two groups, there was non-significant change was observed and the values were within the physiological limit.

The haemoglobin oxygen saturation decreased non-significantly at 15 minutes, 30 minutes and 60 minutes after anaesthesia in both the groups. It started to increase towards normal in both the groups at 120 minutes. There was no significant difference between the groups at all the intervals. Khattri *et al.* (2013) [13] reported a significant decrease in oxygen saturation at 15 and 20 minutes after dexmedetomidine administration in buffalo calves which is possibly due to a certain degree of respiratory depression caused by α_2 agonists. Ahmad *et al.* (2011) [1] did not notice any significant changes at different intervals after administration of dexmedetomidine in dogs.

Haematological Parameter

Heamoglobin (g/dL)

In group-I, the Mean±SE values of hemoglobin was calculated and there was no significant changes were

observed. Similar trend was observed in group-II animals with scheduled time intervals.
Comparison between the groups showed non-significant variation at all interval of schedule.

Packed Cell Volume (%)
In group-I, the Mean±SE values of packed cell volume was calculated and there was no significant changes were observed. Similar trend was observed in group-II animals with scheduled time intervals.
Comparison between the groups showed non-significant variation at all interval of schedule.

Total Erythrocyte Count (×10^6/µL)
In group-I, the Mean±SE values of total erythrocyte count was calculated and there was no significant changes were observed. Similar trend was observed in group-II animals with scheduled time intervals.
Comparison between the groups showed non-significant variation at all interval of schedule.

Total Leucocyte Count (×10^3/µL)
In group-I, the Mean±SE values of total erythrocyte count was calculated and there was no significant changes were observed. Similar trend was observed in group-II animals with scheduled time intervals.
Comparison between the groups showed non-significant variation at all interval of schedule.

Neutrophils (%)
The comparison within the group at different interval revealed that, the nuetrophils count increased significantly between 5 minutes after post-induction and 15minutes after post-anaesthesia when compared to pre-anaesthetic level in both groups, it remained significantly higher level even at 30 minutes after anaesthesia, however it decreased to the physiological limit at 60 minutes after anaesthesia.
The comparison between the groups at different interval revealed that, there was non-significant ($p \geq 0.05$) difference in nuetrophil count.

Heamatological Observations
Statistically there was no significant difference between the groups. The hematocrit values fluctuated within the normal limits throughout anaesthesia in all the animals. In both groups hemoglobin decreased non-significantly however it remained in the physiological limits.
Packed cell volume has no statistical significant difference between the groups and decrease was within the physiological limits during all scheduled intervals.
Total erythrocyte count was non-significant decrease was observed between the group and within the groups and the decrease was within physiological limit in all intervals. The decrease in hemoglobin, packed cell volume and total erythrocyte count values are non-significant and within physiological limit. The results are in agreements with earlier workers (Hikasa *et al.,* 2000, Ajadi *et al.,* 2008, Nuh, 2008 and Abu-Ahmad, 2013) [1, 9, 2, 18]. The decrease in the hematocrit values might be attributed to the combined effect of drugs on venous tone, pooling of blood in spleen, vasodilatation and subsequent hemodilution as observed (Malik and Singh, 2007) [16]. The total leucocyte count (TLC) increased non-significantly within the normal limit in all the intervals. Increase in TLC was observed at maximum depth of anaesthesia in both the groups. Nuetrophilia were recorded in both groups during anaesthesia, it could be due to stress caused by the anaesthetic drug and subsequent stimulation of adrenal gland (Singh *et al.,* 2013) [17].

Table 1: Mean ± SE of physiological parameters at different intervals in cattle of group I and II

S. No	Parameter	Time	Group I	Group II
1	Rectal Temperature (^{0}F)	0min	102.25±0-15^a	101.55±0.23^b
		10min	101.93±0.10	101.93±0.10
		5min	101.65±0.12*	101.65±0.12
		15min	101.10±0.23**	101.10±0.23
		30min	100.53±0.33**	100.53±0.33*
		60min	100.85±0.24**	100.85±0.24
		120min	101.61±0.14	101.65±0.14
2	Respiratory Rate (Breaths/min)	0min	25.80±1.88	25.83±1.83
		10min	19.66±1.62*	19.66±1.62*
		5min	21.33±1.58	21.33±1.58
		15min	24.80±1.27	24.83±1.27
		30min	26.66±1.02	26.66±1.07
		60min	28.33±2.13	28.33±2.13
		120min	32.33±1.49*	32.33±1.49*
3	Heart Rate (Beats/min)	0min	66.16± 1.35	66.16±1.35
		10min	55.50± 1.66**	55.50±1.66**
		5min	58.50±1.70**	58.50±1.70**
		15min	59.82±1.07**	59.83±1.07**
		30min	57.00±1.90**	57.00±2.00**
		60min	59.50±1.90*	59.50±1.91*
		120min	63.00±1,60	63±1.63

Values bearing superscript*differ significantly ($P \leq 0.05$) from interval 'before' within the group.
Values bearing superscript**differ significantly ($P \leq 0.01$) from interval 'before' within the group.
Values bearing superscript ^{a,b} differ significantly ($P \leq 0.05$) level between groups at corresponding intervals

Table 2: Mean ± S.E. of haemodynamic observations at different intervals in cattle of group I and II

S. No	Parameter	Time	Group I	Group II
1	Mean Arterial Pressure (mm of Hg)	0min	85.83±2.71	85.83±2.71
		10min	79.83±3.40	79.83±3.75
		5min	86.05±3.96^a	74.43±4.27^{b*}
		15min	85.10±2.70	85.10±2.71
		30min	88.65±5.05	88.65±5.05
		60min	84.44±2.38	84.44±2.38
		120min	88.66±5.85	88.66±5.85
2	Haemoglobin oxygen saturation (SpO_2) (%)	0min	96.16±1.22	96.16±1.22
		10min	97.16±1.04	97.16±1.04
		5min	96.00±1.48	96.00±1.48
		15min	94.66±1.64	94.66±1.64
		30min	95.66±1.33	95.66±1.33
		60min	93.33±1.76	93.33±1.76
		120min	94.16±1.66	94.16±1.66

Values bearing superscript*differ significantly ($P \leq 0.05$) from interval 'before' within the group.
Values bearing superscript ^{a,b} differ significantly ($P \leq 0.05$) level between groups at corresponding intervals.

Table 3: Mean±SE of Haematological parameters at different intervals in cattle of I and II

S. No	Parameter	Time	Group I	Group II
1	Hb (g/dL)	0min	15.10±0.36	15.10±0.36
		10min	14.96±0.32	14.96±0.32
		5min	14.81±0.33	14.75±0.34
		15min	14.71±0.32	14.71±0.32
		30min	14.45±0.29	14.45±0.29
		60min	14.26±0.30	14.26±0.30
		120min	14.18±0.31	14.18±0.31
2	Packed Cell Volume (%)	0min	40.96±1.11	40.96±1.11
		10min	40.96±1.10	40.96±1.10
		5min	40.81±0.33	40.81±1.09
		15min	40.61±1.12	40.61±1.12
		30min	39.96±1.13	39.96±1.13
		60min	39.78±1.15	39.78±1.15
		120min	39.75±1.13	39.75±1.10
3	TEC ($x10^6$ /µL)	0min	4.75±0.09	4.75±0.09
		10min	4.75±0.09	4.75±0.09
		5min	4.71±0.10	4.71±0.10
		15min	4.67±0.11	4.67±0.10
		30min	4.65±0.10	4.65±0.10
		60min	4.63±0.10	4.63±0.10
		120min	4.62±0.10	4.62±0.10
4	TLC ($x10^3$ /µL)	0min	12.85±0.40	12.85±0.40
		10min	13.00±0.35	13.00±0.35
		5min	13.25±0.34	13.25±0.34
		15min	13.60±0.30	13.60±0.30
		30min	13.80±0.30	13.83±0.30
		60min	13.81±0.31	13.83±0.31
		120min	13.90±0.28	13.90±0.28

Table 4: Mean±SE of Haematological parameters at different intervals in cattle of I and II

S. No	Parameter	Time	Group I	Group II
1	Neutrophils (%)	0min	32.17±2.04	33.00±1.53
		10min	34.50±2.06	35.00±1.67
		5min	42.67±2.35**	44.00±1.67**
		15min	45.67±2.50***	46.83±1.67***
		30min	39.33±3.16**	41.00±2.02***
		60min	33.50±2.58	33.33±2.23
		120min	32.17±2.04	33.00±1.53
2	Lymphocytes (%)	0min	25.45±0.85[a]	21.21±1.19[b]
		10min	25.65±0.84	21.51±1.17
		5min	25.95±0.83	21.83±1.12
		15min	26.40±0.78	22.23±1.14
		30min	26.80±79 [a]	22.71±1.17 [b]
		60min	27.10±0.81[a]	23.00±1.15 [b]
		120min	27.40±0.77	23.50±1.09

Values bearing superscript*differ significantly (P≤0.05) from interval 'before' within the group.

Values bearing superscript [a,b] differ significantly (P≤0.05) level between groups at corresponding intervals.

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