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Effects of romifidine and its reversal with atipamezole in bovine

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Abstract
Twelve clinically affected bovine calves of either sex, weighing 100-150kgs were divided into two groups, containing of 6 calves in each group. Group-I received romifidine @ 40 µg/kg i.m. and group-II received romifidine @ 40 µg/kg, i.m followed by atipamezole @ 40µg/kg i/v at 30 minutes of romifidine sedation. The induction time, duration and recovery time were 7.83±0.34, 91.00±1.96 and 116.33±3.37 minutes respectively in group-I. In group-II, romifidine induced sedation was reversed by injecting atipamezole in 1.07±0.38 minutes. Atipamezole effectively reversed the sedative effects of romifidine at 1.07 ±0.38 min and all the values returned towards the pre-administration level within 15 minutes. Based on the findings of the study, romifidine sedation and its reversal by atipamezole can be suggested for use in clinically affected bovine calves.

Keywords: Romifidine, Atipamezole, sedation, bovine

1. Introduction
Most of the Indian farmers are still dependant on bullock for ploughing, where some of the bullocks are injured requiring immediate surgical intervention. Moreover, fracture is also common among the bullocks as well as dairy cows. In rural areas, open grazing system invites in fighting causing injuries like broken horn are very common. Beyond this, ruminal impaction, traumatic reticulo pericarditis are the cases requiring surgery at the doorstep of farmers. It is difficult to carry gaseous anaesthetic machine to the spot, and injectable anaesthetic play a pivotal role to mitigate such emergencies. Looking to the easy application of injectable anaesthetics, it is contemplated to carry out the research work in bovine. It is essential to reverse the effect of the anaesthetic following completion of the intervention under sedation, which will increase the safety and eliminate the untoward stress of the animal. Quick reversal of the bovine after operation can avoid many of the post-operative complications like tympany and radial paralysis and making the animal fit for normal gait. The present study deals with the clinical, physiological and biochemical changes in bovine calves sedated with romifidine and its reversal with atipamezole

2. Materials and Method
Twelve numbers of bovine calves of different age groups of either sex, weighing 100 to 150 kgs belonging to some private owners brought to the Department of Surgery and Radiology, College of Veterinary Science, AAU, Khanapara, Guwahati with various ailments and requiring surgical interventions like castration, dressing of wounds, drainage of abscess, repair of bone fracture etc. were divided into two groups. Group I received romifidine @ 40 µg/kg i.m. and in group II, romifidine @ 40 µg/kg i.m. followed by atipamezole @ 40 µg/kg i.v., 30 minutes after romifidine administration. Feed and drinking water were withheld for 24 hours and 12 hours respectively, prior to injection of these drugs.
Induction time, duration of sedation and recovery time were studied in all the calves. Atipamezole was injected intravenously at the peak of sedation produced by romifidine and the recovery time was recorded with sitting from recumbency, standing with ataxia and complete recovery with walking. Heart rate, respiration rate, rectal temperatures, tidal volume, minute volume, mean arterial pressures and partial pressures of oxygen were recorded at 0, 15, 30, 45, 60 and 90 minutes of injection of romifidine and also after injection of atipamezole too. Five ml of venous blood was collected at 0, 15, 30, 45, 60 and 90 minutes of romifidine injection and of which 2ml were collected in EDTA vial for haematological estimation and 3 ml were collected in a clot activator vial and serum was separated for estimation of different

biological parameters. GGT, Glucose, BUN, creatinine, and total protein were estimated using standard methods. The data were statistically analysed by using windows based statistical package *viz* Microsoft Excel and SPSS 16.0.

3. Results and Discussion

The animals of group-I, which received Romifidine @40 µg/kg body weight exhibited induction time, longer duration and recovery time as 7.83±0.34 minutes, 91.00±1.96 minutes and 116.33±3.37 minutes, respectively. In the animals of group II, alpha-2-adrenoceptor antagonist atipamezole was administered intravenously at the peak of romifidine sedation i.e. at 30 minutes of romifidine injection, Atipamezole effectively reversed the anaesthetic action where the reversal time recorded was 1.07±0.38 minutes for recumbency and at 2.59±0.57 min standing with ataxia and complete recovery with walking at 3.44±1.08 minutes. Romifidine produced sedation was of sufficient duration required for most of the surgical intervention in elephant reported by Talukdar *et al.* (2012) [11]. Even after completion of operation the calves were lying in the ground. But in the second group, following use of atipamezole reversal the calves totally recovered from sedation, not allowing untoward situation like radial paralysis and ruminal atony. Atipamezole is a specific alpha-2-antagonist which could effectively reversed the romifidine induced sedation in calf. This finding was in agreement with the findings of Sharma *et al.* (1996) [10] in calves following intravenous administration of atipamezole to reverse the sedative effects of medetomidine. Similar findings were also reported by Gogoi *et al.* (2002) [1].

There was significant (P<0.05) decreased in the heart rate in the calves of group-I from 64.00±1.29 to 40.83±0.70 beats/minute at 45 minutes following administration of romifidine which thereafter returned towards the base values, but remained lower than the pre-administration values. However, in the group II following administration of atipamezole as reversal at 30 minute of romifidine sedation, the heart rate increased non-significantly (P>0.05) from 40.83±1.09 to 59.79±1.16. Antagonism of romifidine by atipamezole raised the sympathetic outflow and thereby caused increase in the heart rate after its administration in romifidine sedated calves. This was in agreement with the findings of Mahmood and Fouad (2008) [5] by using atipamezole in goats sedated with medetomidine, another member of same group drug. Martin and Rebecca (2015) [6] observed return of cardiac output to baseline levels following administration of atipamezole in dogs sedated with dexmedetomidine.

In the animals of group I, respiration rate decreased significantly (P<0.05) from 16.83±1.25 to 10.83±0.65 per minute and the maximum depression was recorded at 30 minutes of romifidine administration, which gradually returned towards base value. In the second group following intravenous administration of atipamezole, the respiratory rate increased significantly (P<0.05) from 11.23±1.67 to 14.67±1.51 at 15 minutes of atipamezole which was near normal and this reduction of respiratory rate was in agreement following Romifidine-Ketamin injection into Asian Elephant (Sarma and Choudhury, 2011) [8] might be due to the antagonistic effects of atipamezole on romifidine induced sedation. Ndeerch *et al.* (2001) [7] also reported similar findings after administration of antagonist drugs in xylazine sedated goats. Significant increase in the respiratory rate recorded in the study was corroborated well with the findings of Sarma and Pathak (2004) [9] in medetomidine-ketamine induced sedation in Asian elephants.

The rectal temperature decreased significantly (P<0.05) in group I throughout the period of study after receiving romifidine. This decrease in rectal temperature might be accredited to decrease in basal metabolic rate, depression of the thermoregulatory centre in the brain and muscle relaxation. However, in the animals of group II following administration of atipamezole, temperature increased non-significantly (P>0.05) and remained higher for the subsequent period of study. It might be due to faster antagonistic effects of atipamezole on romifidine which was in support of the findings of Mahmood and Fouad (2008) [5] following intravenous administration of atipamezole in medetomidine sedated goats.

There was significant (P<0.05) declination of respiratory tidal volume and respiratory minute volume in the animals of group I with maximum declination at 60 minutes. However, in the animals of group-II reversal with atipamezole at the peak of romifidine sedation lead to almost static respiratory tidal volume and minute volume in the remaining period of study. Ko *et al.* (1996) [4] also reported that there were no significant alteration of tidal volume in dog after administration of atipamezole as at the peak of medetomidine sedation in dogs.

The mean arterial pressure decreased significantly (P<0.05) in group-I from 123.67±4.12 to 107.00±4.34 at 30 minutes, thereafter it increased (113.17±3.38) significantly (P<0.01) till the end of the experiment. In the group II, where atipamezole was injected intravenously at 30 minutes of romifidine sedation exhibited gradual increase of MAP from 110.30±1.15 to 132.00±0.73 till the end of the study period and the increase was found to be statistically significant (P<0.05). It might be due to antagonistic effects of atipamezole on romifidine, where MAP increased sharply incomparison to the group-I.

In group I, the S_PO_2 values decreased significantly (P<0.05) from 99.17±0.31 to 91.17±0.70 at 45 minutes and thereafter returned towards the base value at the end (96.67±0.56) of the study. However, following atipamezole administration, S_PO_2 level increased non-significantly (P>0.05) from 91.23±0.56 to 99.31±0.33 in group-II, which might be due to the faster antagonistic effect of atipamezole on romifidine. Jalanka (1989) [3] reported similar findings using atipamezole as reversal in medetomidine-ketamine induced immobilization in snow leopard.

The haemoglobin level decreased non-significantly (P>0.05) in the animals of group-I up to 60 minutes from the pre-administrative levels of 9.65±0.21 to 9.15±0.16 g/dl. However, in group-II following atipamezole administration, haemoglobin level increased non-significantly (P>0.05), which might be due to the antagonistic effect of atipamezole on romifidine. This finding was in accordance with the observations made by Gogoi *et al.* (2002) [1] preceding atipamezole administration in medetomidine anaesthetized goats.

In the animals of group-I, PCV decreased non-significantly (P>0.05) from a pre- administration level of 31.66±1.05 to 27.50±0.67% upto 60 minutes. Whereas, in group-II, resulted non-significant (P>0.05) increase in PCV from 28.67±0.56 to 31.97±0.48. This gradual change after atipamezole administration might be due to the release of erythrocytes into the circulation, attributed to the contraction of the enlarged spleen by atipamezole which had been earlier

caused by romifidine. Gohain (2008) [7] also reported similar findings following intravenous administration of atipamezole in Asian elephants.

Non-significant (P>0.05) decrease in TEC was recorded from 7.10±0.20 to 6.64±0.24 (million/cu mm) and this decrease was continued till the end of the study, which did not show any tendency to return towards the base value. However, in the group-II, there was TEC increased non-significantly (P>0.05) following administration of atipamezole. This increased after atipamezole administration might be due to the release of erythrocytes into the circulation, attributed to the regained normal tonacity of the relaxed spleen. The result was in accordance with the findings of Gohain (2008) [7] following the use of atipamezole to antagonise the effect of medetomidine in Asian elephant.

A non significant (P>0.05) variation of the erythrocyte sedimentation rate following romifidine was observed among the animals of group-I. However, there were non-significant (P>0.05) variation of ESR in the animals of group II, after administration of atipamezole. It might be due to antagonistic effects of romifidine by intravenous administration of atipamezole.

Highly significant (P<0.01) increase in GGT levels was recorded following romifidine up to 60 minutes in group-I, which sharply declined thereafter towards the base values. In the animals of group-II, GGT decreased significantly (P<0.05) after atipamezole. It might be due to antagonistic effects of atipamezole, which was in support of the findings of Gogoi *et al* (2002) [1].

Serum glucose levels increased significantly (P<0.05) upto 60 min in group-I from 117.29 ± 6.03 to 63.43±1.35 (m/dl) and thereafter returned towards normal at the end of the experiment. In group-II, after the administration of atipamezole there was non-significant (P>0.05) decrease in serum glucose levels but the values remained above the base values till the end of the observation period. Similar observation was also reported by Gohain (2008) [7] in Asian elephant by using atipamezole to antagonise the effect of medetomidine.

The BUN increased significantly (P<0.05) in group-I from 26.98±0.67 to 43.49±1.78 at 30 minutes of romifidine administration and then returned gradually towards pre-administration levels at the end of the study. In the animals of group-II after administration of atipamezole, BUN decreased non-significantly (P>0.05). Gohain (2008) [7] was also in support of the findings of the present study, where BUN decreased after atipamezole

Creatinine level increased non-significantly (P>0.05) from 1.36±0.11 to 1.49±0.11 at 30 minutes in group-I and gradually returns towards the pre -administration level at the end of the observation. In group-II, after the administration of atipamezole there was non-significant (P>0.05) decrease in creatinine level. This was in agreement with the findings of Gohain (2008) [7] after the intravenous administration of atipamezole to reverse the effect of medetomidine in Asian elephant.

In group I animals, total protein decreased non-significantly (P>0.05) from a pre-administration level of 61.13±2.82 to 58.36±2.75 g/dl at 60 minutes and returned thereafter towards the pre -administration level by the end of the observation. The animals of group II after atipamezole reversal exhibited non-significant (P>0.05) increase in total protein but remained within the physiological limit till the end of the observation period. Gohain (2008) [7] also recorded similar effect following intravenous injection of atipamezole to reverse the effects of medetomidine in Asian elephants.

4. Conclusion

After conducting this study in clinically affected bovine calves, it could be concluded that romifidine @ 40µg/kg produced sufficient sedation and atipamezole @ equal amount of romifidine successfully reversed the sedative effects of romifidine within a very short time. Therefore, romifidine sedation and atipamezole as a reversal can be suggested for use in clinically affected bovine calves.

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