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Some haematological changes in goats following restraint and reversal using medetomidine and atipamezole

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Abstract
The influence of pharmacological restraint of Sokoto red goats by medetomidine and its reversal with atipamezole was investigated. Four different treatment protocols were studied, that is medetomidine singly at 10 and 20µg/kg and the same doses followed after 15minutes by atipamezole at 40 and 80µg/kg respectively by IM route. The results indicated that the heamoglobin concentration, PCV and TLC were all significantly altered from the normal values for some intervals following treatment. The interval of significant reduction was prolonged when medetomidine was administered without reversal. Administration of atipamezole significantly shortens the duration of reduction of the parameters. The hematological traits were not significantly different from the baseline values at 24 hours in all treatment groups, indicating that no permanent alteration has been induced. The reversibility of the altered haematological parameters means these drugs are safe in goats presented for surgery.

Keywords: Medetomidine, atipamezole, Sokoto red goats, pharmacological restraint, haematological traits

Introduction
The blood is the medium in which important constituents are distributed to all parts of the body, it usually contain high concentrations of many endogenous and xenobiotic substances. Drugs following administration usually attain high concentrations in the blood and this could have profound effects on the outcome of drug therapy and health status of animals.
Medetomidine is an alpha 2 adrenoceptor agonist more potent than xylazine and detomidine with which it shares a lot of pharmacological profile [1]. Parenterally administered medetomidine produce a dose dependent influence on haemodynamic parameters [2] Medetomidine has been evaluated and found to be effective in the sedation of goats [3-6]. Under its CNS depressant influence the rate of adaptive changes in response to stress to maintain homeostasis is impaired. Several studies has been undertaken in goats to investigate influence of medetomidine singly or in combination on the blood [7-9]. It is therefore very important to investigate the influence of medetomidine on some haematological traits in the Sokoto red goats a local breed of goat noted for its prized skin. Atipamezole has also been noted to reverse many pharmacological effects of medetomidine [10, 11]. It is the aim of the present study to investigate the effects of sedative doses of medetomidine on some hematological parameters and the possible reversal of same by atipamezole in Sokoto red goats.

Materials and Methods
Animals: Eight Sokoto Red goats consisting of four males and four non- pregnant non-lactating females were used. The goats were 2-3 years of age and 14-22kg of weight. They were housed separately according to sex in two goat pens and had free access to feed and water. Feed was withheld for 12h prior to the commencement of the experiment.

Drugs: Medetomidine (Domitor®) 1mg/ml veterinary injection and atipamezole (Antisedan®) 5mg/ml veterinary injections (Orion Corporation Animal Health, Turku, Finland) were used in this study.

Study Design: The study was carried out using eight treatment protocols. Eight goats equally divided between the sexes were given each treatment in a randomized design with seven days washout period.

The treatment protocols were

1. Medetomidine 10µg/kg
2. Medetomidine 20µg/kg
3. Medetomidine 10µg/kg followed by atipamezole 40µg/kg
4. Medetomidine 20µg/kg followed by atipamezole 80µg/kg

Medetomidine and atipamezole doses used in this study were as previously determined to be effective [11]. All drug administrations was through the intramuscular route. The baseline values were used as controls.

Blood Sampling: Pre-sedation blood samples were taken by jugular venepuncture and at 30, 60, 120, 180, 300 minutes and 24 hours later. The blood was aspirated into specialized capillary tubes for hematological estimations. This was done electronically using the QBC II Centrifugal hematology system model 0221(Becton Dickinson Primary Diagnostics U.S.A).

For the purpose of this study only the PCV, TLC and hemoglobin concentrations values were recorded.

Statistical Analysis: Data were analyzed, using ANOVA, and pair wise comparisons were made, using least-significant difference multiple comparison test. All data are presented as mean ±SD and $P<0.05$ was considered significant.

Results

The effects of the four treatment protocols on hemoglobin concentrations are presented (Figure 1). Following treatments 1 and 2 the hemoglobin concentrations decreased significantly at all sampling times between 30th and 120th minutes post medetomidine administration. The hemoglobin concentrations from 180th minutes upwards was however not significantly different from the baseline values.

The influence of medetomidine sedation and its reversal with atipamezole on PCV is presented (Figure 2.) Following treatments 1 and 2 there were significant decreases in mean PCV at 30th and 60th minutes respectively. The decrease following treatment 2 was slightly but non-significantly more than with treatment 1. In treatments 3 and 4 significant changes were observed in PCV values at all sampling times compared to the baseline values.

The influence of the four treatment protocols on TLC is presented (Figure 3) In treatments 1 and 2 there were significant decreases in the TLC at 30th, 60th and 120th minutes following drug administration. At all subsequent sampling times till 24 hours no significant changes of TLC were recorded. In treatments 1 and 2, the lowest TLC were obtained at 60th minute following drug administration and they were $7.0\pm0.3x10^3$ and $6.5\pm0.5x10^3$ respectively. No significant changes in TLC were obtained in treatments 3 and 4 at all sampling times. No permanent alterations in the haematological traits were evident 24 hours post drug administration.

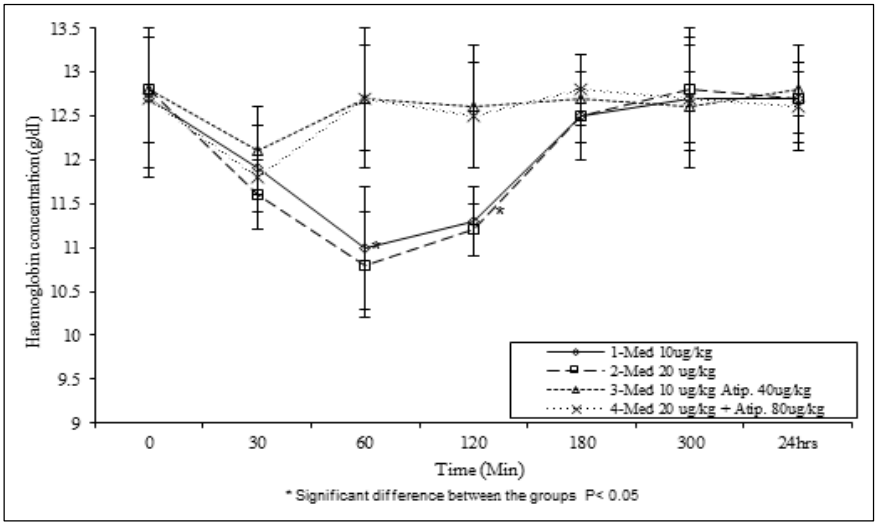

Fig 1: Haemoglobin concentration (g/dl) (Mean ± Sd) following medotomidine sedation and its reversal with atipamezole in SRG

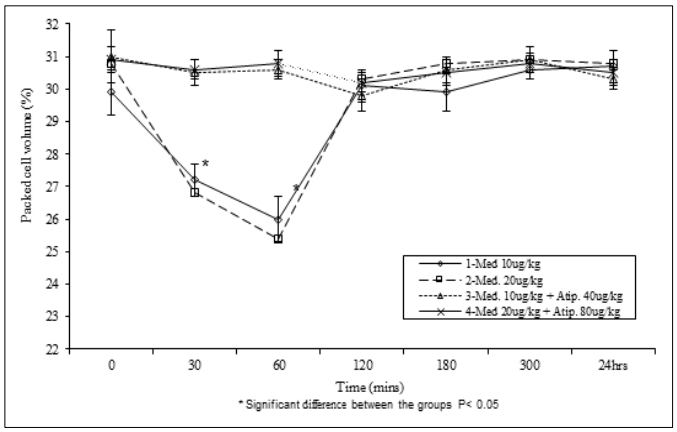

Fig 2: Packed cell volume (%) (Mean ± SD) following medetomidine sedation and its reversal with atipamezole in SRG

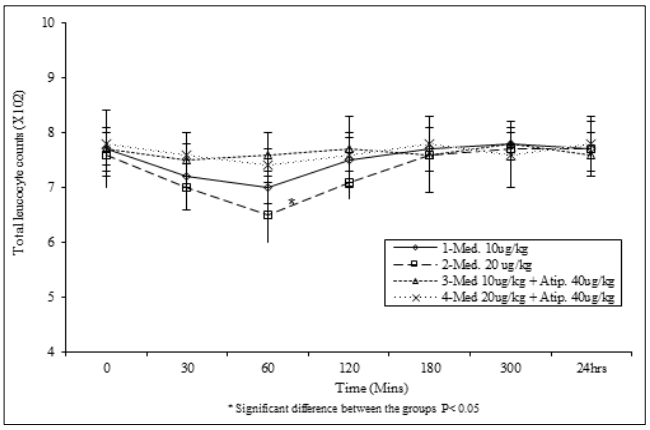

Fig 3: Total leucocyte counts ($x10^2$) (Mean ± SD) following medetomidine sedation and its reversal with atipamezole in SRG

Discussions

There were significant reductions in haemoglobin (Hb) packed cell volume (PCV) and total leucocyte counts (TLC) folowing medetomidine sedation. The significant reductions in these haematological traits were found to be transient in nature, reverting back to the baseline values shortly. This concurred with previous reports with medetomidine in goats and wild ruminants [4, 8, 9, 12-16]. It has been reported that erythrocyte counts, haematocrit values and haemoglobin concentrations in cattle and dogs have shown significant but reversible decreases following xylazine administration [17, 18].

The lowered values of haemoglobin and PCV in medetomidine-sedated goats may be due to hypotension, which could cause the entry of interstitial fluids into the circulation, thus producing haemodilution. It has been demonstrated in several studies that α_{2-} adrenoceptor agonists induce sustained lowering of blood pressure following an initial hypertension [19-21].

Apart from changes in plasma volume, changes in the number of circulating erythrocytes may also contribute to reduction of PCV as earlier suggested [22, 23]. Splenic dilatation and variable pooling of erythrocytes in the tissue that is known to be reservoir for the cells has been the basis of a drop in PCV with barbiturates and propofol [24, 25].

The decrease in PCV following xylazine has been attributed to increase pooling of blood into the spleen [26]. There has been a suggestion that xylazine cause haemolysis [27]. Anaesthetics- induced depression of the haematological parameters has been reported in mammals [28-30]. These changes are thought to be caused by anaesthetic-induced splenic vasodilation resulting in pulling of blood cell from the vessels [31]. The actual mechanisms responsible for the lowering of the haemoglobin concentration, TLC, and PCV in this study remain obscure.

Atipamezole effectively reversed the decrease as shown in treatments 3 and 4 following medetomidine in this study. It has been suggested that the α_{2-} adrenergic blocking properties of acetylpromazine cause relaxation of the splenic capsule, sequestration in PCV, and induces a decrease in total plasma protein, secondary to vasodilation and haemodilution [8, 9, 32].

The decrease in total leucocyte count (TLC) in this study may also be attributable to haemodilution. However, leucopenia observed during the peak effect of pentobarbitone has been attributed to the pooling of leucocytes into the lungs [33]. Whether this could possibly explain the decrease in TLC in this study remains unclear. Precautions would still be needed in haemodynamically compromised patients, but this study has provided some guide for safe use of these drugs. Some other factors not considered in this study, such as environmental temperature and season of the year may affect some of these variables.

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