

Research Article

Electrocardiography, Blood Pressure Measurements, Vital Parameters and Anaesthetic Indices in the African Giant Rat (*Cricetomys Gambianus* Waterhouse) Immobilized with Diazepam or Ketamine

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Summary: In spite of the increasing use and importance of the African giant rat (*Cricetomys Gambianus* Waterhouse) in research, and other fields, like location of landmines, there is still not enough information on their physiology. In this study, we assessed the electrocardiogram, blood pressure, vital parameters and anaesthetic indices of the African giant rat (*Cricetomys Gambianus* Waterhouse), both genders, using diazepam or ketamine as chemical restraints. A total of 24 adult African Giant Rats (AGR), 12 males and 12 females were used in this experiment. The animals were divided into two groups of twelve animals each (6 males and 6 females). One group was assessed for the effect of diazepam, and the other group ketamine. Diazepam (Roche®, Switzerland) was administered intraperitoneally at a dose rate of 7.5 mg/kg, while ketamine was administered intraperitoneally at a dose rate of 45 mg/kg. Parameters measured were recorded from the time desirable sedation was achieved, and every 15 minutes till the animal was awake. Animals administered diazepam took a longer time to sleep or achieve desirable sedative state, a longer time to respond to stimuli before waking up fully and a longer time to be fully awake, relative to ketamine-induced sedation. Ketamine caused a continuous increase in respiratory rate and blood pressure, while diazepam caused a continuous decrease in the respiratory rate. Electrocardiogram showed tachycardia throughout the experiment with the use of both drugs, although this was more pronounced with the use of diazepam, causing a decrease in QRS interval and a decrease in QT interval. Gender differences were observed in most parameters measured. Results obtained gave baseline values for electrocardiogram and blood pressure readings, while also detailing the changes and gender differences observed with sedation. In addition, results indicated ketamine is best used for short procedures and diazepam at a higher dose used for procedures requiring longer time in the African giant rat.

Keywords: African giant rat, electrocardiogram, blood pressure, diazepam, ketamine, anaesthetic indices.

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INTRODUCTION

The African Giant Rat, (AGR) belongs to the Order Rodentia, Family Nesomyidae, Genus *Cricetomys*. Scientific name *Cricetomys Gambianus* Waterhouse 1840 (Happold, 1987). It is the largest mammalian order with approximately 2016 species in 28 families including squirrels, beavers, chipmunks, rats, mice, lemmings. Gerbils, porcupines, cavies and the capybara. About 50% of the species of living mammals are reported to be rodents (Sheets, 1989). In Africa, these rats are considered to be a delicacy, and are therefore hunted for food. They are high in protein, and are increasingly becoming of interest (Ajayi *et al.*, 1978). More importantly, this rodent has been shown to have a good potential for use as a laboratory animal (Dipeolu *et al.*, 1981) and also, the rodent has been used to

detect tuberculosis in patients and to sniff out landmines (Lindow, 2001).

In animals as active as the AGR, the use of chemical restraint is indicated while handling. Chemical restraint reduces excitement and hyper-activity trauma that may occur during handling, thereby reducing morbidity and mortality (Neiffer *et al.*, 2009). Diazepam and ketamine are anaesthetic drugs used to achieve a sedative or anaesthetic effect.

Diazepam, a benzodiazepine, is used clinically as a muscle relaxant, anticonvulsant, anxiolytic and a sedative-hypnotic (Gavish *et al.*, 1999). It is one of the most common sedatives in use, and it comes in different preparations – oral (tablets), injectable, inhalation and rectal forms (Mikota *et al.*, 2005). Ketamine is an NMDA receptor antagonist (Harrison *et al.*, 1985). It is a drug used in human and veterinary medicine, primarily for the induction and

maintenance of general anaesthesia, usually in combination with a sedative. At high, fully anaesthetic level doses, it has also been found to bind to μ -opioid receptors type 2 in cultured human neuroblastoma cells – however, without agonist activity (Hirota *et al.*, 1999) – and to sigma receptors in rats (Narita *et al.*, 2001). Other uses include sedation in intensive care, analgesia (particularly in emergency medicine), and treatment of bronchospasm. This drug has been reported to have a wide range of effects in humans, including analgesia, anaesthesia, hallucinations, elevated blood pressure, and bronchodilation (Peck *et al.*, 2008). Like other drugs of its class, such as tiletamine and phencyclidine (PCP), ketamine induces a state referred to as "dissociative anaesthesia" (Bergman, 1999), and is used as a recreational drug.

Despite the abundance of information on various aspects of the biology of the African Giant Rat (Adeyemo *et al.*, 1990; Oke *et al.*, 1995, 1999; Ali *et al.*, 2008; Akinloye, 2009; Olude *et al.*, 2011; Salami *et al.*, 2011; Akinloye *et al.*, 2012), there currently exists no information on the cardiological parameters of this animal such as electrocardiography and blood pressure measurements. This study was conducted to evaluate the ECG, BP, vital parameters and anaesthetic indices in the AGR immobilized with diazepam or ketamine.

MATERIALS AND METHODS

Ethical approval was obtained from the Ethical Committee, Faculty of Veterinary Medicine, University of Ibadan, Nigeria, ethical code number 02/14/01. All animals were humanely handled to ensure that they were not caused undue pain or stress, and all experiments were performed in accordance to the guidelines by the National Institute of Health (NIH), USA, and the Animal Care, Use and Research Ethics Committee (ACUREC), University of Ibadan, Nigeria. In addition, all methods were reported in

accordance with ARRIVE guidelines for reporting of animal experiments.

A total of twenty-four (24) apparently healthy animals (12 males and 12 females) were used for this study. The animals were determined to be adults as earlier described using the weight (Ajayi *et al.*, 1978). They were housed in individual, but similar cages designed for the AGR, at the Giant Rat House. Acclimation to their new environment was done for two weeks prior to the commencement of the study. The rats were divided into two groups of 12 rats each (6 males and 6 females), one group to assess the effect of diazepam, and the other group to assess the effect of ketamine.

Sedation of experimental animals and recording of parameters: The rats in the first group were immobilised with 7.5mg/kg of Diazepam (Roche®, Switzerland), intraperitoneally while rats in the second group were immobilised with ketamine at the dosage of 45mg/kg intraperitoneally. The length of time to induce sedation was recorded. Parameters such as the electrocardiogram, blood pressure readings, respiratory rate, and rectal temperature were obtained from the time desirable sedation was achieved, and for every 15 minutes till the time the animal recovered from sedation.

Electrocardiography: Using a 6/7 lead computer ECG machine, (EDAN VE1010, Shanghai, China) lead-II electrocardiograms were recorded as earlier described by Omobowale *et al.* (Omobowale *et al.*, 2017). The machine was calibrated at a paper speed of 50mm/s and vertical at 20mm/mV. Briefly, each animal was placed on right lateral recumbency and the limbs were carefully positioned perpendicularly to the long axis of the body. Parameters such as heart rate, P-wave duration, PR-interval, QRS duration, R-amplitude and QT-interval and QTc (Bazett) were recorded (Fig. 1).



Plate 1: An African giant rat sedated and placed on right lateral recumbency, showing the placement of the ECG electrodes. Note the blood pressure cuff on the tail (black arrow)

Electrocardiogram and blood pressure of the giant rat

Rectal temperature and Respiratory rate: Values for the rectal temperature were obtained with the aid of a digital clinical thermometer and recorded in OC, while the respiratory rate was determined manually using a stop watch, and recorded as number of respirations / minute.

Blood Pressure Monitoring: Placing of cuffs: Blood pressure was monitored with a digital occlimetric blood pressure monitor, model VET400A (Krutech®). The cuff was placed on the cranial aspect of the tail, close to the sacro-caudal joint (of the vertebral column) (Figure 1).

Statistical Analysis

All data obtained were analysed using Graphpad Prism® version 5 (GraphPad Software Inc., La Jolla, CA USA).

Student’s ‘t’ test was used to test significant difference and p<0.05 was accepted as statistically significant.

RESULTS

Body Weight: The body weights (expressed as Mean ± Standard deviation) of the 12 AGRs used to assess the effect of diazepam was 826.7 ± 169.3 grams, with the males having a body weight of 863 ± 184.5 grams and the females 790.3 ± 160.8 grams. The ketamine group had a body weight of 836.7 ± 178.7 grams, with the males being 871 ± 206.7 grams, and the females 802 ± 157.2 grams. No statistically significant difference was observed in the weight of the two groups (p>0.05).

Other results are shown in Table 1 and Figures 2 – 7.

Electrocardiogram: Results are presented in Table 1.

Table 1:
LEAD-II ECG parameters in AGR administered diazepam and ketamine

Parameter	Diazepam				Ketamine			
	0 min	15 min	30 min	45 min	0 min	15 min	30 min	45 min
Heart Rate (/min)	259.2 ± 38.0	268.8 ± 37.9	266.6 ± 42.5	276.0 ± 40.3	178.2 ± 50.0	171.1 ± 46.0	184.2 ± 36.63	213.5 ± 13.4
P-wave duration (ms)	30.3 ± 2.0	37.6 ± 12.3	30.9 ± 6.4	28.8 ± 7.1	28.2 ± 4.3	29.8 ± 6.0	29.4 ± 4.83	27 ± 1.4
P-R interval (ms)	55.4 ± 7.1	57.7 ± 13.4	56.3 ± 7.43	51.3 ± 7.0	52.2 ± 8.6	55.4 ± 7.8	55.2 ± 14.27	47 ± 8.5
QRS duration (ms)	30.3 ± 7.0	29.9 ± 6.9	27.6 ± 10.50	23.5 ± 6.8	32.5 ± 10.7	31.6 ± 8.0	28.6 ± 5.86	26.5 ± 7.8
QT segment (ms)	109.4 ± 18.4	98.2 ± 11.0	89.6 ± 12.0	84.3 ± 2.4	101.5 ± 15.8	97.9 ± 16.0	91.6 ± 17.18	88 ± 2.8
QTcB(ms)	225.1 ± 35.1	206 ± 19.0	187.9 ± 30.8	179.8 ± 10.5	172.6 ± 37.3	163.8 ± 37.0	158.8 ± 30.6	165.0 ± 0.0
R-amplitude (mV)	0.368 ± 0.15	0.372 ± 0.20	0.358 ± 0.17	0.389 ± 0.21	0.370 ± 0.2	0.408 ± 0.17	0.353 ± 0.11	0.365 ± 0.2

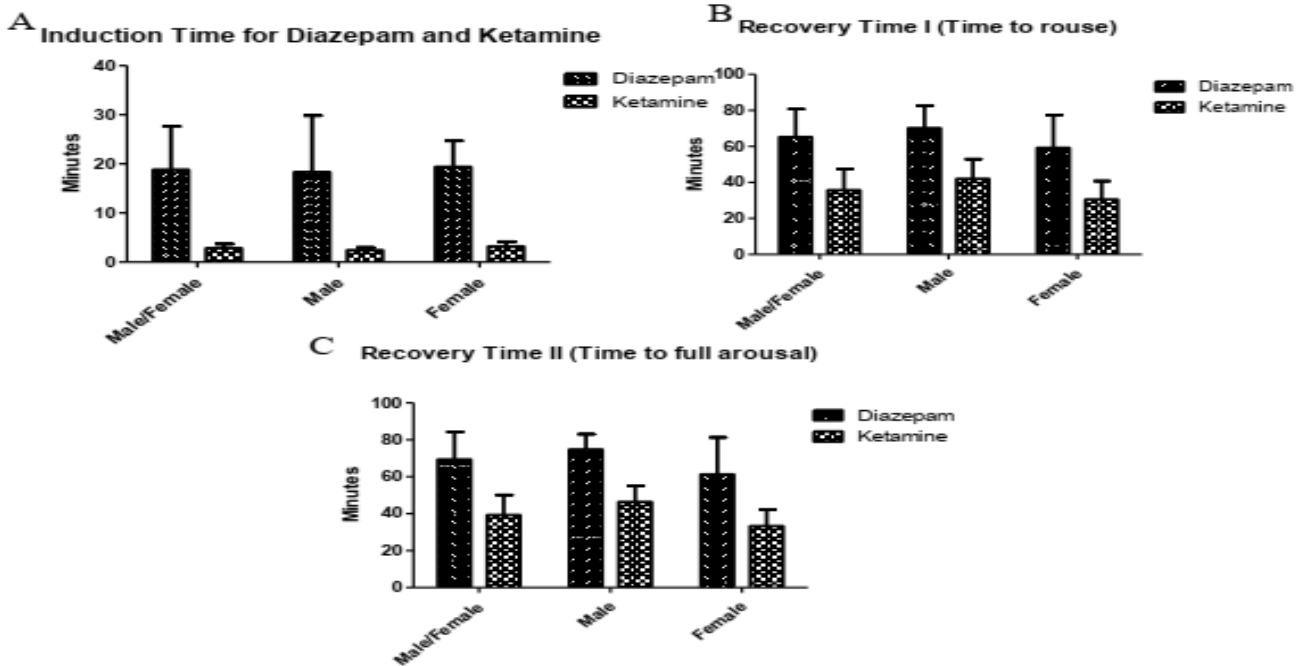


Figure 2A-C: Bar charts showing time to induce sedation (A), time to arouse from sedation (B), and time to arouse completely from sedation (C), using diazepam or ketamine in AGR. Male/Female (n = 12), Male (n = 6) and Females (n = 6). Values obtained for ketamine were statistically significantly lower (p<0.05) in A – C, although values obtained for the males with ketamine administration was statistically significantly higher than the females (p<0.05) in C.

Both diazepam and ketamine caused an increase in the heart rate. Diazepam caused an increase, then a decrease in the P-wave duration. Ketamine caused the same change in the P-wave duration, although not as pronounced. This trend was also observed in the P-R interval. A progressive decrease was observed with the use of the two drugs in the QRS duration, the QT segment and the QTcB. The pattern observed for the R-amplitude was similar in both cases. At $p < 0.05$, statistical significance was observed in the heart rate values between diazepam and ketamine at 0, 15 and 30 minutes ($p < 0.05$), but not at 45 minutes ($p > 0.05$). QTcB using the two drugs showed statistical significance at 0, 15 and 45 minutes ($p < 0.05$). A decrease in QRS duration was observed from 0 to 45 minutes, with the use of both drugs.

Time to induce desirable sedation and time to recover from sedation (induction and recovery times): This was recorded in minutes (Figures 2A-C).

Statistically significant difference was observed between the time it took to achieve desirable sedation (induction time), the length of time from when the animal slept off to when it started to wake up, or respond to stimuli (recovery time I) and the length of time from when the animal slept off to when it was fully awake and could move around (recovery time II/ time to full arousal) values for diazepam versus ketamine ($p < 0.05$). Comparing male values with female values revealed statistical significance for time to attain full arousal, when ketamine was used, with the males having higher values (46.4 ± 8.71 minutes) relative to the females (33.33 ± 8.96 minutes) ($p < 0.05$).

With the use of diazepam, at 15 minutes, all the animals (100%) were still sedated. At 30 minutes, 11 animals remained sedated (91.7%, of the AGR population, 100% male population, 83.3% female population). At 45 minutes, 7 animals (5 males, 2 females) remained sedated (58.3% of the AGR population, 33.3% of the females, and 83.3% of

the males). Only one animal, male (16.7% of the male population, and 8.3% of the AGR population), remained sedated for up to 60 minutes throughout the experiment. This was during the administration of diazepam.

During ketamine sedation, at 15 minutes, all animals (100%) remained sedated. At 30 minutes, 7 animals remained sedated (4 males and 3 females) – 58.3% of the total AGR population, 66.7% of the male population and 50% of the female population. At 45 minutes, only two animals (both males) remained sedated (33.3% of the male population and 16.7% of the total AGR population).

Blood Pressure

Systolic Blood Pressure: Results are presented in Figures 3A-C. Ketamine appeared to result in a progressive increase in the systolic pressure of all the animals, both male and female. This is unlike that observed in diazepam-induced sedation where the males showed an increase, but the females recorded a decrease before an increase

Diastolic Blood Pressure: Results are presented in Figures 4A-C. As was observed in the systolic pressure, ketamine maintained a progressive increase in diastolic pressure, the pattern of which was similar in both male and female. Diazepam caused an initial increase, followed by a drop, and finally an increase. In the male, diazepam caused an increase in the last 15 minutes of the experiment (30 to 45 minutes), but a further decrease in the females for the last 15 minutes.

Mean Arterial Pressure: Results are presented in Figures 5A-C. Ketamine resulted in a progressive increase in the mean arterial (MA) pressure, also expressed in the same way in both genders. Diazepam caused an increase, a decrease and finally an increase, as was observed in the diastolic pressure in males.

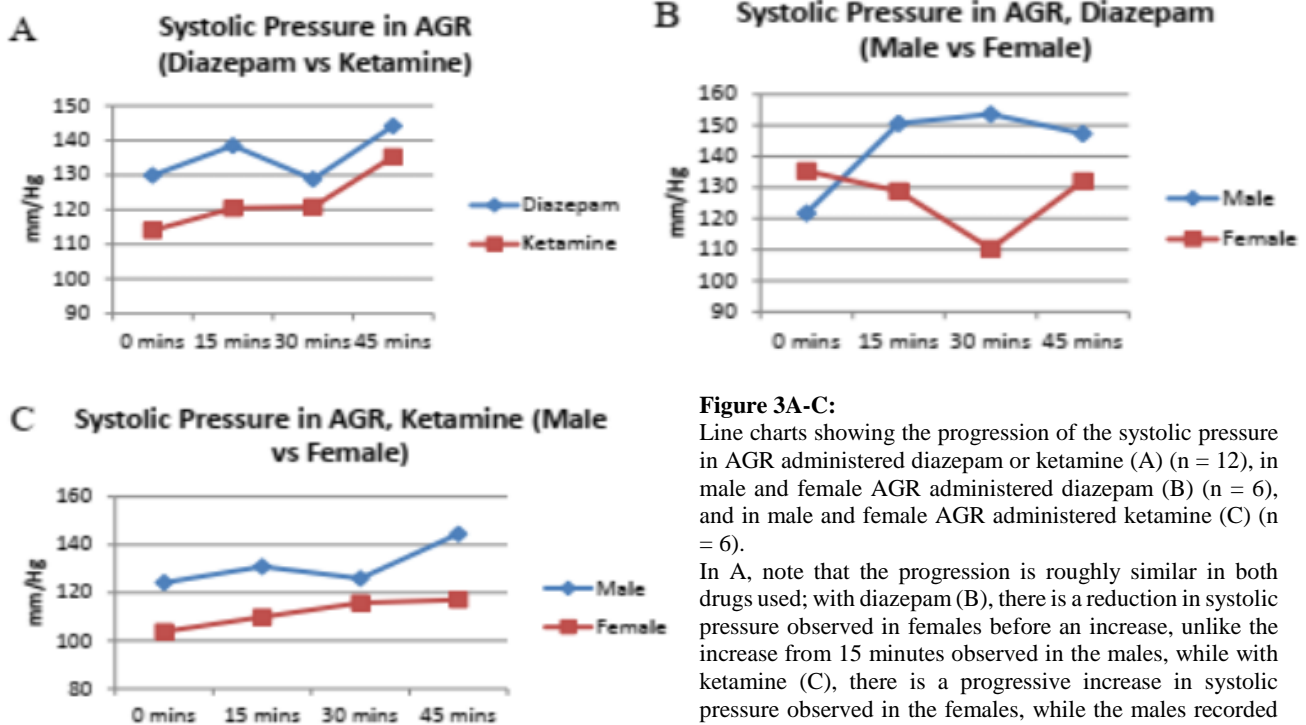


Figure 3A-C:

Line charts showing the progression of the systolic pressure in AGR administered diazepam or ketamine (A) ($n = 12$), in male and female AGR administered diazepam (B) ($n = 6$), and in male and female AGR administered ketamine (C) ($n = 6$).

In A, note that the progression is roughly similar in both drugs used; with diazepam (B), there is a reduction in systolic pressure observed in females before an increase, unlike the increase from 15 minutes observed in the males, while with ketamine (C), there is a progressive increase in systolic pressure observed in the females, while the males recorded an increase, followed by a decrease, and finally, an increase.

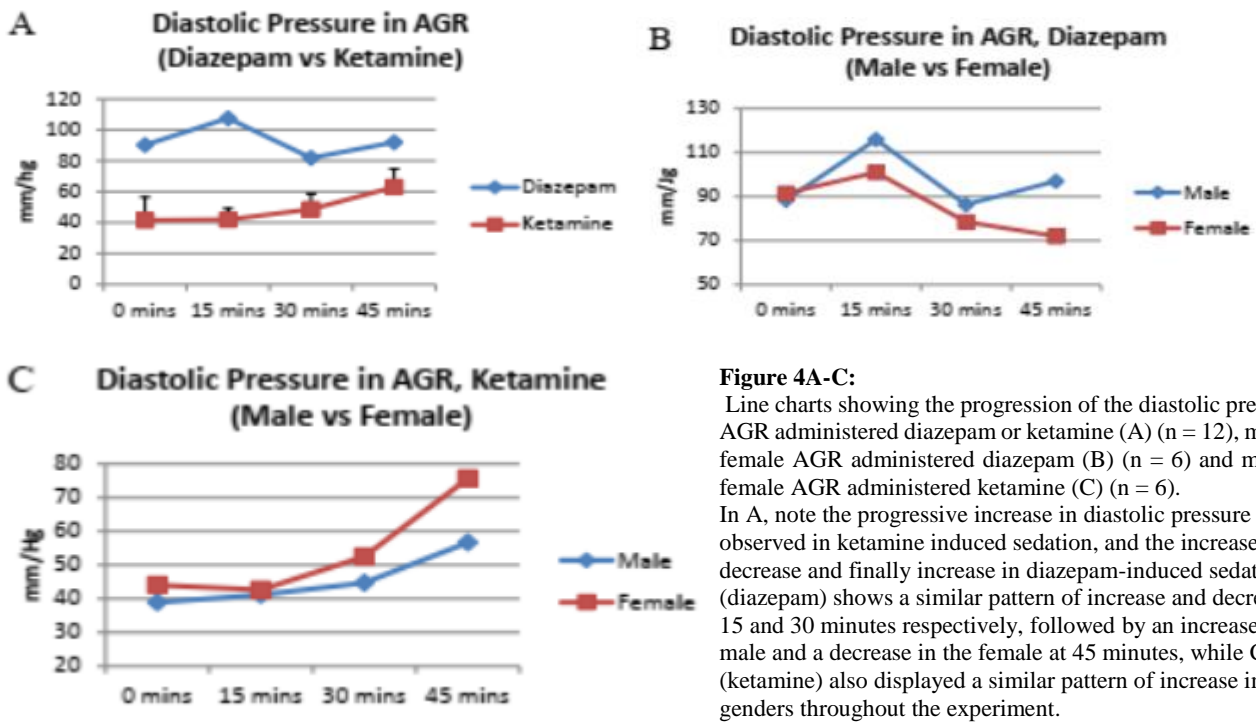


Figure 4A-C:

Line charts showing the progression of the diastolic pressure in AGR administered diazepam or ketamine (A) (n = 12), male and female AGR administered diazepam (B) (n = 6) and male and female AGR administered ketamine (C) (n = 6). In A, note the progressive increase in diastolic pressure observed in ketamine induced sedation, and the increase, decrease and finally increase in diazepam-induced sedation. B (diazepam) shows a similar pattern of increase and decrease at 15 and 30 minutes respectively, followed by an increase in the male and a decrease in the female at 45 minutes, while C (ketamine) also displayed a similar pattern of increase in both genders throughout the experiment.

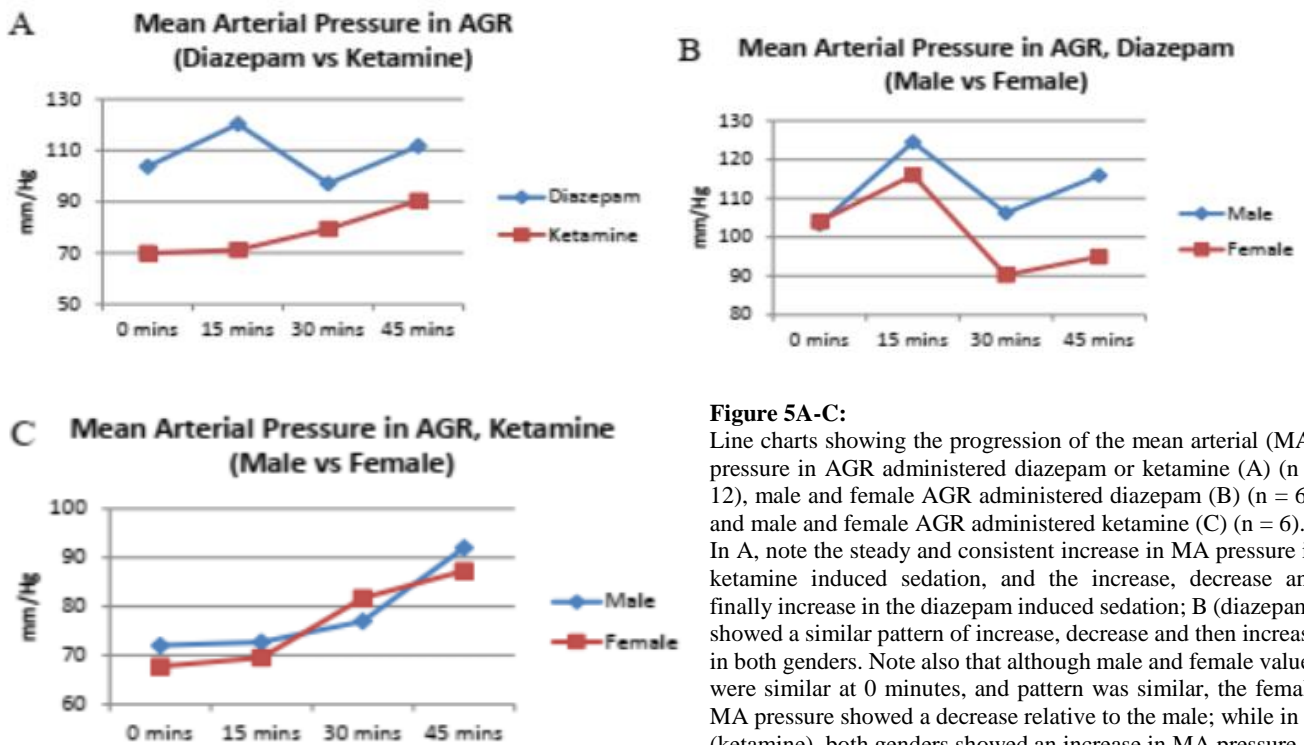


Figure 5A-C:

Line charts showing the progression of the mean arterial (MA) pressure in AGR administered diazepam or ketamine (A) (n = 12), male and female AGR administered diazepam (B) (n = 6), and male and female AGR administered ketamine (C) (n = 6). In A, note the steady and consistent increase in MA pressure in ketamine induced sedation, and the increase, decrease and finally increase in the diazepam induced sedation; B (diazepam) showed a similar pattern of increase, decrease and then increase in both genders. Note also that although male and female values were similar at 0 minutes, and pattern was similar, the female MA pressure showed a decrease relative to the male; while in C (ketamine), both genders showed an increase in MA pressure.

Respiratory Rate: Results are presented in Figures 6A-C. Ketamine administration resulted in an increase in the respiratory rate while diazepam depressed it very slightly, although no significantly significant difference was observed between the two drugs. In comparing the genders, diazepam administration resulted in an increase in respiratory rate in the females, with a slight decrease

observed at 30 minutes. The males however, showed a decrease in respiratory rate. Ketamine-induced sedation in the females showed an increase (15 mins), and then a slight decrease (30 mins), while the males had an increase up till the 45-minute mark. All ketamine-administered rats were awake before 60 mins.

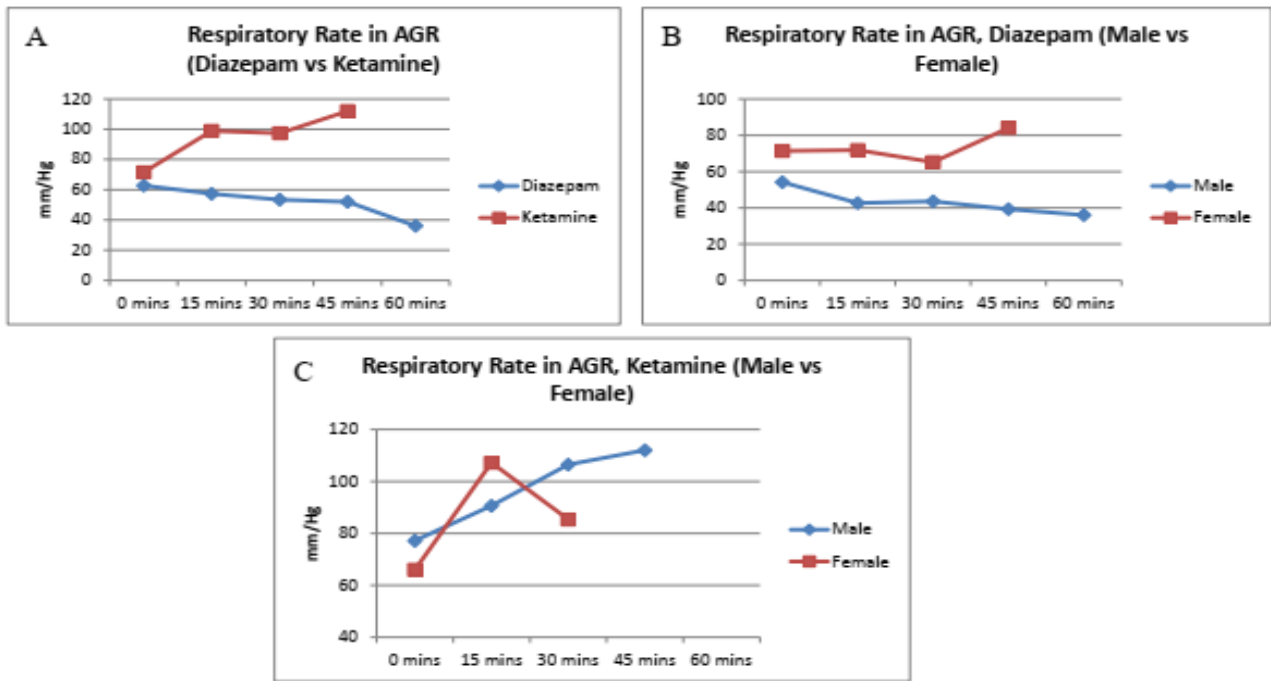


Figure 6A-C:

Line charts showing progression of respiratory rate in AGR administered diazepam or ketamine (A), male and female AGR administered diazepam (B) and male and female AGR administered ketamine (C).

In A, note the increase in respiratory rate in the ketamine group relative to the decrease in the diazepam group. No value was available for ketamine at 60 minutes, as all animals were fully awake by then; in B (diazepam), note the increase in respiratory rate in the females, although a slight dip occurred at 30 minutes. The males showed a depression or decrease in respiratory rate relative to the females; while in C (ketamine), there was an increase at 15 minutes, and then the dip at 30 minutes in values obtained in the females. The males showed a progressive increase in the rate of respiration up to 45 minutes. No animal hit the 60-minute mark.

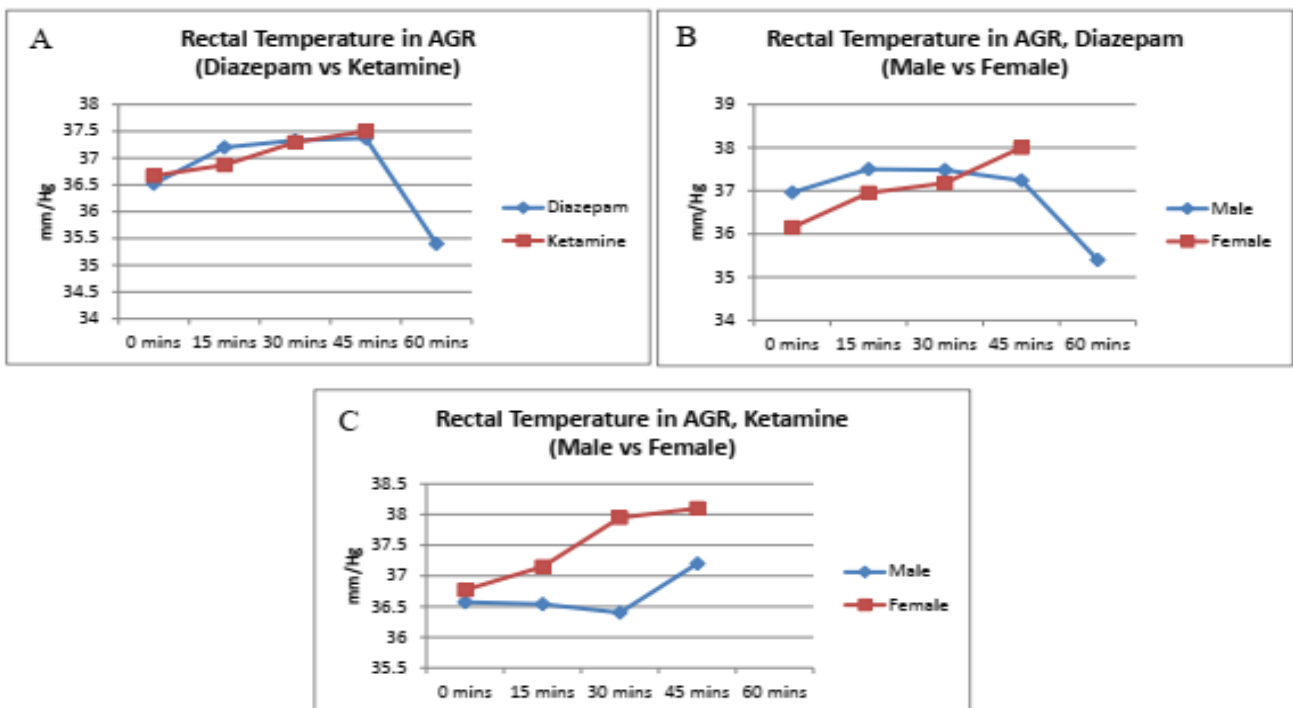


Figure 7A-C:

Line charts showing rectal temperature (Tr) in AGR administered diazepam or ketamine (A), male and female AGR administered diazepam (B) and male and female AGR administered ketamine (C).

In A, note the increase in both diazepam and ketamine up to 45 mins, and the subsequent decrease at 60 mins in the diazepam group. In B (diazepam), there was a consistent increase in Tr in the females, unlike the males. Also, all females were awake before 45 mins. In C (ketamine), the females also showed a consistent increase, while the males showed a slight decrease before an increase. All animals were awake before the 60 mins mark.

Rectal Temperature: Results are presented in Figures 7A-C. In both males and females, using diazepam or ketamine, an increase in temperature was observed. The rate of increase was observed to decrease as the time was progressing towards the wearing off of sedation. By 60 minutes (observed for a single animal – male), a sharp decrease was observed in the value of the rectal temperature. Progression of temperature was observed to be similar with the use of the two sedatives. With the use of diazepam, progression of temperature change in both genders was similar till 30 minutes post-administration. By 45 minutes, an increase in temperature of 0.90°C was observed in the female, while a drop in temperature of 1.80°C was observed in the male. It should be noted however, that only a single male made it to the 60 minutes mark.

With the use of ketamine, the females showed a progressive increase in rectal temperature up to 45 minutes, while the males showed a slight drop from 0 to 30 minutes, which increased from 30 to 45 minutes. No statistically significant difference was observed between values for diazepam and ketamine, and the time frames (0, 15, 30, 45 and 60 minutes) ($p > 0.05$).

DISCUSSION

In this study, males had a higher mean body weight than the females. This observation is consistent with earlier reports in the fruit bat (Igado *et al.*, 2012) and that of Campbell (Campbell, 1990), who had earlier on made an observation that the males of most species are usually heavier than the females.

Anaesthetic management and handling of wildlife is often a challenge encountered by veterinarians or scientists. Ketamine at 45 mg/kg induced desirable sedation in a time considerably and statistically significantly lower ($p < 0.05$) than diazepam (7.5 mg/kg). In spite of the fact that ketamine induced sedation faster, the period of sedation was considerably lower than that of diazepam, and the animals recovered faster from ketamine-induced sedation.

Ketamine is 10 times more lipid soluble than thiopentone and can quickly cross the blood-brain barrier. This makes it relatively rapid in the onset of effect and recovery due to redistribution, similar to the thiobarbiturates. The onset of anesthesia/sedation, in one study, was 45 seconds after intravenous injection (2 mg/kg) and 4 minutes after intramuscular injection (3 mg/kg) with recovery times of 18 minutes and 25 minutes respectively (Cotsen *et al.*, 1997). After intravenous injection in humans, the distribution half-life [$t(1/2\pi)$] was 24.1 seconds, redistribution half-life [$t(1/2\alpha)$] was 4.68 minutes, and elimination half-life [$t(1/2\beta)$] was 2.17 hours (Domino *et al.*, 1984) (Domino *et al.*, 1984). In our current study, ketamine (45 mg/kg) administered intra-peritoneally, gave an induction time of 2.818 ± 0.87 minutes, and recovery times of 35.73 ± 11.7 and 39.27 ± 10.82 minutes.

Ketamine at approximately 40 mg/kg body weight by intramuscular injection was shown to provide sedation that waned over approximately one hour (Fowler *et al.*, 2008). Flecknell (Flecknell, 1996) found that a combination of medetomidine (0.5 mg/kg) and ketamine (75 mg/kg) by intraperitoneal injection provided effective anaesthesia (although not necessarily for major surgery) in rats. In this

current study, diazepam gave a longer period of sedation, but the sedative effect was not as effective as that of ketamine. This implies that ketamine is probably ideal for short procedures, while diazepam, at higher doses may probably be used for longer procedures, or in combination with other drugs.

Homeotherms (birds and mammals) employ physiologic mechanisms to maintain their body temperature within a narrow range, despite constant exothermic metabolism and wide ambient temperature fluctuations (Gordon, 2009). The rectal temperature is a good indicator of the core body temperature that is widely used in animals because of its accuracy, convenience and safety (Keim *et al.*, 2002; Zhao *et al.*, 2010). The rectal temperature of the AGR in this study did not display any statistically significant change, indicating that these drugs do not result in temperature changes. The decrease in temperature observed at some points may be due to the inactivity of the animal due to sedation. Also, it should be noted that the ambient temperatures on the days of the experiment remained relatively constant. The current experiment was carried out during the harmattan season (October to January), and results obtained were found to be similar to and within the same range as that obtained by Dzenda *et al.*, (Dzenda *et al.*, 2011), during the dry season (34.07 to 39.77°C). It is noteworthy however, that the highest temperature obtained in the current experiment (39.0°C), observed in a male during diazepam administration, was still lower than the maximum obtained by Dzenda *et al.*, (Dzenda *et al.*, 2011) in harmattan (39.77°C), and the hot dry season (36.31°C to 40.15°C).

Based on the fact that results obtained with the two drugs administered were still within the range of normal rectal temperatures obtained during seasonal investigations in previous studies (Dzenda *et al.*, 2011), it can be safely deduced that neither diazepam nor ketamine exerted any significant change in the rectal temperature of the AGR. Diazepam was observed to suppress the respiratory rate while ketamine elevated it. This is contradictory to Heshmati (Heshmati *et al.*, 2003), who reported that ketamine suppresses breathing more than other available anaesthetics. According to Peck *et al.*, (Peck *et al.*, 2008), ketamine causes bronchodilation, which may probably be responsible for the increased respiratory rate observed in ketamine induced sedation. This was more obvious in the males than the females who had a decrease in respiratory rate at 30 minutes. The reason for this decrease in respiratory rate needs further investigation to ascertain probable gender differences in response of AGR to ketamine.

Male and female response to diazepam in this study differed greatly, as the females recorded an elevation in respiratory rate, and the males, a depression. The reason for this could not be ascertained, and no record of gender difference in the reaction to diazepam could be obtained. Respiration, heart rate, blood pressure and level of consciousness are controlled by numerous nuclei in the brainstem (Purves *et al.*, 2004). It is possible that the two drugs used in this experiment elicited differing responses from the respiratory centres.

The systolic pressure graph for diazepam and ketamine followed a similar pattern except for the decrease in diazepam at 30 minutes. An increase in systolic pressure

was also observed in both genders with the use of ketamine. Diastolic and mean arterial pressures were also observed to increase with the use of ketamine. This is consistent with the findings of West *et al.*, (West *et al.*, 2007) and Peck *et al.*, (Peck *et al.*, 2008), that ketamine causes increased mean arterial blood pressure and blood pressure respectively. This makes ketamine a drug to be considered in hypotensive animals, in cases of hypovolemic shock and in patients where blood volume status cannot be ascertained. No appreciable difference was observed between the male and the female, implying that ketamine might not necessarily cause gender specific reactions when administered, unlike what was observed with the use of diazepam.

Although diazepam caused an increase, then a decrease followed by an increase in systolic pressure, this trend was not the same when gender differences were considered. Diazepam showed a decrease in systolic pressure in the females, with an increase resulting at 45 minutes, unlike in males, where an increase was observed from 0 minutes. This same pattern was observed in the diastolic and mean arterial pressures. There was a great similarity between the male and female in mean arterial pressure with the use of diazepam. Results obtained may indicate the risk of hypotension at 30 minutes with the use of diazepam, in both sexes. This depression is consistent with the decrease in respiratory rate observed with the use of diazepam. Results from this experiment differs a bit from the findings of Kitajima *et al.*, (Kitajima *et al.*, 2004), that diazepam like all benzodiazepines cause hypotension (significant decrease of systolic and mean arterial blood pressure) by a central mechanism. Kitajima *et al.*, (Kitajima *et al.*, 2004), administered diazepam (5mg) intravenously to human subjects. The difference in this current experiment and the previous experiment may be due to difference in subjects (AGR versus humans). This may also show that AGR react differently to diazepam when compared with other subjects. This may need further investigation, in view of the increasing awareness of the AGR as a laboratory animal. Ketamine resulted in an increase in blood pressure, coupled with an increase in respiratory rate, making it a seeming ideal drug for use in cases of respiratory arrest, in asthmatic patients or in cases of chronic obstructive pathway (Lankenau *et al.*, 2007). It can be concluded that when diazepam is to be used, more care should be employed in monitoring blood pressure and respiration.

The increase in heart rate in both groups can be attributed to one or more of the following mechanisms: a decrease in vagal tone, an increase in sympathetic tone, an increase in circulating catecholamines and a direct effect on the cardiac pacemaker and conduction (Dennis *et al.*, 2007). The duration of electrical conduction through atrioventricular node (PR interval) was similar between the diazepam and ketamine groups, implying that both drugs can result in delayed atrioventricular conduction when administered at a dose to result in prolonged sedation. There was a decrease observed in the QRS duration with the administration of diazepam and ketamine, from 0 minutes to 45 minutes. This may mean that the two drugs may cause a shortening of the interventricular and His bundle conduction times (Weber *et al.*, 1995). In dogs, QT interval was reported to be inversely related to the heart rate (Oguchi *et al.*, 1993). This is evident in this study as the heart rate was observed to increase while the QT interval decreased.

During the administration of ketamine, all animals were observed to have their eyes open throughout the period of sedation. Ketamine produces a unique anaesthetic state (dissociative anesthesia), characterized by dissociation between the thalamocortical and limbic systems. Patients are usually unconscious and cataleptic or partially conscious but unable to respond purposefully to physical stimulation or verbal command, depending on dose. Their vital reflexes are generally intact but can be depressed. Therefore, by definition, ketamine produces a unique state somewhere between deep sedation and general anesthesia (Bergman, 1999). This ability of ketamine to make patients partially conscious, but unable to respond to physical stimulation or verbal command may have been responsible for the non-closure of eyelid in spite of the fact that the animal appeared reasonably sedated.

During diazepam induced sedation, the animals were observed to move their mouths in a chewing manner. Also, upon recovery from diazepam sedation, they were observed to reach immediately for their food bowls. Diazepam has been reported to be used occasionally as an appetite stimulant. It is said to induce hyperphagia via a GABAergic action (Rahminiwati *et al.*, 1999). This may be responsible for the observed seemingly increased desire for food.

In conclusion, this study assessed the ECG readings, blood pressure values and vital parameters of the AGR. These values could not be obtained without sedation, therefore anaesthetic indices were recorded. Results obtained will provide baseline data in the field of internal medicine and surgery for these animals and other similar rodents.

The use of diazepam (7.5 mg/kg) and ketamine (45mg/kg) in the AGR may be ideal for short non-surgical procedures (when used without combination with other drugs). In order to make the animal more fully anaesthetised for surgery, higher doses may be recommended, or the use in combination with any other appropriate anaesthetics. With the increased use of these animals for research, further investigations need to be carried out to fully determine the reactions of this unique animal to these drugs, and the merits and demerits there are.

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