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Evaluation of the effect of piroxicam and ascorbic acid combination on live weight and rectal temperature of savannah brown goats during post-operative pain management

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The aim of the study was to evaluate effects of varied doses of ascorbic acid (AA) and piroxicam on live weight (LW) and rectal temperature (RT) responses in orchidectomised savannah brown goats during post-surgical pain management. The goats were divided into six groups of three goats each. Orchidectomy was performed on all animals under sedation with xylazine, and linear infiltration with lignocaine. Post-surgery, varied doses of piroxicam (IM) and AA (IV) were administered to the goats: Group A = piroxicam, 5 mg/kg + AA, 100 mg/kg; Group B = piroxicam, 5 mg/kg + AA, 200 mg/kg; Group C = piroxicam, 10 mg/kg + AA, 100 mg/kg; Group D = piroxicam, 5 mg/kg; Group E: AA, 100 mg/kg together with procaine penicillin, (20,000 IU/kg) + streptomycin (10 mg/kg) (IM); and Group F (control) received only the antibiotics. Post-surgery, RT was measured with the use of an auto-physiologic monitoring machine and LW with weighing scale. Goats in the control group showed decreased LW and RT increase. Treatment with a combination of piroxicam and AA ameliorated LW and temperature more than either of the agents in orchidectomised savannah brown goats.

Keywords: piroxicam; ascorbic acid; live weight; rectal temperature; pain

1. Introduction

An important trend in goat research is the central role the interplay between nutrition and pathology plays (Argüello 2011). It has been suggested that changes in temperature, respiratory rate and feeding behaviour are of value in pain assessment (NRC 2008). Live weight (LW) is an important index of stress in livestock (Minka & Ayo 2007, 2010). Pain can be assessed by the measurements of the activity of the sympathetic nervous system (Molony & Kent 1997). The measurements include changes in cardiovascular (altered heart rate, changes in pulse quality and decrease in peripheral circulation) respiratory parameters (abnormal breathing pattern, altered rate and depth), pupillary diameter and skin resistance (Morton & Griffiths 1985). In Recent times, new facts and knowledge about drugs is emerging in goat science (Argüello 2011). Piroxicam is a non-steroidal anti-inflammatory drug (NSAID). It has been widely used to treat podagrous and rheumatoid arthritis, gonarthrosis, osteoarthritis, backaches, neuralgia, mialgia and other diseases accompanied by pain syndrome or an inflammatory process (Kormosh et al. 2011). Piroxicam is primarily used to treat arthritis and other musculo-skeletal conditions (Agrawal & Gupta 2010). It exhibits anti-inflammatory, anti-rheumatoid arthritis (Hedner et al. 2004), analgesic (Izdes et al. 2003) and antipyretic activities in animal models. The mechanism of action of piroxicam, like any NSAID, is not completely understood, but may be related to prostaglandin synthetase inhibition (Abdallah et al. 2011).

Ascorbic acid (AA), also known as vitamin C, is an essential micronutrient that is acquired primarily through the consumption of fruits, vegetables, supplements, fortified beverages and fortified breakfast or 'ready to-eat' cereals (World Health Organisation 2006). It is an effective antioxidant that plays an important metabolic role in the body. By acting as an electron carrier, it gives up two electrons and is converted to dehydro-L-AA (Whitehead & Keller 2003). AA mitigates negative effects of stress (Minka & Ayo 2007, 2010, 2013) and protects body cells from the deleterious effects of reactive oxygen species (ROS) and mutagens (Powers & Jackson 2008; Yarube et al. 2009). Hanck and Weiser (1985) reported a dose-dependent pain reduction by oral administration of AA in rats. The ROS play a crucial role in neuropathic pain (Kim et al. 2004). AA alters the clinical parameters and sleeping time in rabbits under xylazine anaesthesia (Egwu et al. 2011). Castration has been described as the commonest surgical procedure in both large and small animals (Fadason et al. 2007; Remi-Adewunmi & Gyang 2010). It reduces aggression (towards other animals), improves handler safety, reduces sexual behaviour and improves

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Table 1. Experimental grouping of animals.

Group	Treatment protocol
A	Piroxicam at 5 mg/kg (IM) and AA at 100 mg/kg (IV), penicillin 20,000 IU/kg and streptomycin, 10 mg/kg (IM)
B	Piroxicam at 5 mg/kg (IM) and AA at 200 mg/kg (IV), penicillin 20,000 IU/kg and streptomycin, 10 mg/kg (IM)
C	Piroxicam at 10 mg/kg (IM) and AA at 100 mg/kg (IV), penicillin 20,000 IU/kg and streptomycin, 10 mg/kg (IM)
D	Piroxicam at 5 mg/kg (IM) and penicillin 20,000 IU/kg and streptomycin, 10 mg/kg (IM)
E	AA at 100 mg/kg (IV), penicillin 20,000 IU/kg and streptomycin, 10 mg/kg (IM)
F (control)	Penicillin 20,000 IU/kg and streptomycin 10 mg/kg (IM)

Group A – Animals administered with piroxicam at 5 mg/kg (IM) and AA at 100 mg/kg (IV), penicillin 20,000 IU/kg and streptomycin, 10 mg/kg (IM).
Group B – Animals administered with piroxicam at 5 mg/kg (IM) and AA at 200 mg/kg (IV), penicillin 20,000 IU/kg and streptomycin 10 mg/kg (IM).
Group C – Animals administered with piroxicam at 10 mg/kg (IM) and AA at 100 mg/kg (IV), penicillin 20,000 IU/kg and streptomycin, 10 mg/kg (IM).
Group D – Animals administered with piroxicam at 5 mg/kg (IM) and penicillin 20,000 IU/kg and streptomycin, 10 mg/kg (IM).
Group E – Animals administered with AA at 100 mg/kg (IV), penicillin 20,000 I.U/kg and streptomycin, 10 mg/kg (IM).
Group F (control) – Animals administered with penicillin 20,000 I.U/kg and streptomycin, 10 mg/kg (IM).

meat quality (González et al. 2010; Coetzee 2011). The common methods of castration in food animals include: (1) orchidectomy, which is the removal of the testicles after making an incision into the scrotum; (2) band or ring castration, which involves constricting the blood supply to the testicles and scrotum; and (3) Burdizzo castration, which involves crushing of the spermatic cord. The ability to perform castration with certainty is important because failure to do so will result in castration being performed at an older age (Stafford 2007), when the pain and complications due to the procedure may be more severe. According to both the American and Canadian Veterinary Medical Associations (AVMA and CVMA, respectively), the castration methods cause both acute and chronic pain (AVMA 2006; CVMA 2011). Prunier et al. (2005) showed that during pain, ROS are generated in large quantity. Antioxidants such as AA may, therefore, be beneficial in pain alleviation during surgical interventions in animals.

The aim of the present study was to evaluate the LW and rectal temperature (RT) responses in goats, orchidectomised and administered with piroxicam and AA during post-surgical management of pain.

2. Materials and methods

2.1. Experimental animals

Ethical approval letter for the conduct of this experiment, with reference no VSR 12/005, was obtained from the Research Ethics Committee of the Department of Veterinary Surgery and Radiology, Ahmadu Bello University, Zaria, Nigeria. Eighteen, six-month to one-and-half-year-old savannah brown goats, weighing between 6 kg and 12 kg were used. The goats were pre-conditioned for a period of five weeks, during which general clinical and behavioural evaluations were conducted on the animals to determine their baseline data before post-operation evaluation. Goats were given access to feeds (hay, beans husk and maize offals) and clean water *ad libitum.* The goats were divided into six experimental groups of three goats each (Table 1). Castration (orchidectomy) was performed on all the goats.

2.2. Pre-surgical preparation, anaesthesia and restraint

The scrotal area was shaved, scrubbed with soap and water and disinfected with chlorhexidine. The animals were sedated with 0.05 mg/kg xylazine (XYL-M2®, VMD n.v/s.a-Hoge Mauw 900-B-2370 Arendonk, Belgium) intravenously. Local anaesthesia was achieved through a linear infiltration with 5 ml of 2% lidocaine hydrochloride (Liga®, SAI Parenterals (P) Ltd., Hyderabad-55, India), subcutaneously into the scrotal sac. The animal was then restrained in dorsal recumbency in a surgical cradle, and the scrotum and the surrounding area were disinfected with chlorhexidine (Fubini & Ducharme 2004). The probes from the auto-physiologic monitoring machine (Gen. Meditech Inc., Model G3D) were attached to the goats; surgical area was then draped for surgery.

2.3. Surgical procedure

The scrotum was grasped and a horizontal incision made through the skin and the fascia at the widest part of the scrotum; that is the junction of idle and distal thirds. The entire distal segment of the scrotum was transected and traction placed on the testes and the skin pushed proximad. The fascia was separated from the spermatic cords, enclosed in the common tunics with care taken to avoid the proximal regions of the spermatic cords. The spermatic cords were ligated by transfixation suture, using size 2 chromic catgut and the cord transected distal to the ligatures according to the method described by Simon and Wayne (1992). Cutaneous wounds in goats were dressed using topical antibiotics, oxytetracycline aerosol spray, containing

Gentian violet + Oxytetracycline (Sequent Scientific Ltd., Thane, India). Procaine penicillin, 20,000 IU/kg and streptomycin, 10 mg/kg (Centre-Prodih®, Aether Centre Biology Co., Ltd., Beijing, China) were administered intramuscularly for five consecutive days post-surgery. This group (F) served as the control. The same procedures, comprising Surgery, Oxytetracycline spray, procaine penicillin and streptomycin were carried out on all the animals in Groups A–F.

Goats in Group A were given Piroxicam (piroxicam®) (Laborate Pharmaceutical, E-11 Industrial area, Panipat-123 103, India) at 5 mg/kg intramuscularly and AA (ECNU-C Injection®, Yanzhou Xierkangtai Pharmaceutical Co. Ltd., Yanzhou City, China) at 100 mg/kg intravenously for five consecutive days post-surgically.

Group B goats were given piroxicam at 5 mg/kg intramuscularly and AA at 200 mg/kg intravenously for five consecutive days post-surgically.

Goats in group C were given piroxicam at 10 mg/kg intramuscularly and AA at 100 mg/kg intravenously for five consecutive days post-surgically.

Piroxicam was administered at 5 mg/kg intramuscularly for five consecutive days post-surgically to goats in Group D.

Group E goats were given AA at the dose rate of 100 mg/kg intravenously for five consecutive days. Post-surgery, pain intensity was determined in each goat using their behavioural responses graded according to numerical rating scale (Bourne & Forbes 2005).

2.4. LW measurement

The weight of each goat was measured before surgery, and the values obtained served as the baseline data. The animals were weighed immediately after surgery, three hours after surgery and every other day for five consecutive days. The weights were measured when a person mounted on the weighing scale and his personal weight was noted and recorded. A goat was then handed over to him and the weight of 'both' noted and recorded. The difference between the person's weight and the weight of both the person and the goat served as the weight of the animal.

2.5. RT measurement

The RT of each goat was determined by measuring the RT immediately, three hours and daily for five days post-surgery using an auto-physiological parameter monitoring machine (General Meditech Inc., model G3D, Guangdong, China). Probe from the machine was inserted into the rectum and the temperature recorded. The records were taken at 09:00 hours, for five consecutive days post-surgery.

2.6. Statistical analyses

LW and RT values are shown in Tables 2, 3 and 4. Data obtained were expressed as mean ± standard error of the mean (Mean ± SEM). They were analyzed using one-way analysis of variance with Tukey's multiple comparison *post-hoc* test, using GraphPad version 4.0 for windows (GraphPad Software, San Diego, California, USA) to compare the level of significance between the tests.

3. Results and discussion

A decrease in body weight was observed in the experimental animals immediately and three hours after

Table 2. Body weight of goats (kg) administered with different concentrations of piroxicam, AA and streptomycin/penicillin (n = 3; Mean ± SEM).

	Group A	Group B	Group C	Group D	Group E	Group F
Baseline	7.5 ± 1.0	8.2 ± 0.9	9.5 ± 1.3	8.3 ± 0.7	8.3 ± 1.9	9.8 ± 1.1
Immediately after surgery	7.3 ± 0.93	7.8 ± 0.88	9.5 ± 1.0	8.0 ± 0.76	8.0 ± 1.9	9.3 ± 0.83
3 hours post-surgery	7.2 ± 0.88	8.2 ± 0.93	9.5 ± 1.3	8.0 ± 0.76	8.0 ± 1.6	9.2 ± 0.93
Day 1	7.7 ± 0.83	7.8 ± 1.2	9.5 ± 1.3	8.0 ± 1.0	8.5 ± 1.7	8.5 ± 0.76
Day 2	7.7 ± 0.88	8.2 ± 0.73	9.3 ± 1.2	8.0 ± 0.58	8.2 ± 1.6	8.2 ± 0.93
Day 3	7.5 ± 0.76	8.3 ± 0.88	9.0 ± 1.5	8.3 ± 0.67	8.3 ± 1.6	8.7 ± 1.2
Day 4	7.2 ± 0.73	8.2 ± 1.0	9.5 ± 1.3	8.3 ± 0.67	8.2 ± 1.5	8.3 ± 0.83
Day 5	7.7 ± 0.83	8.3 ± 0.88	9.5 ± 1.3	8.2 ± 0.60	8.5 ± 1.6	8.8 ± 1.1

Group A – Animals administered with piroxicam at 5 mg/kg (IM) and AA at 100 mg/kg (IV), penicillin 20,000 IU/kg and streptomycin, 10 mg/kg (IM).
Group B – Animals administered with piroxicam at 5 mg/kg (IM) and AA at 200 mg/kg (IV), penicillin 20,000 IU/kg and streptomycin, 10 mg/kg (IM).
Group C – Animals administered with piroxicam at 10 mg/kg (IM) and AA at 100 mg/kg (IV), penicillin 20,000 IU/kg and streptomycin, 10 mg/kg (IM).
Group D – Animals administered with piroxicam at 5 mg/kg (IM) and penicillin 20,000 IU/kg and streptomycin, 10 mg/kg (IM).
Group E – Animals administered with AA at 100 mg/kg (IV), penicillin 20,000 I.U/kg and streptomycin, 10 mg/kg (IM).
Group F (control) – Animals administered with penicillin 20,000 I.U/kg and streptomycin, 10 mg/kg (IM).

Table 3. Percentage LW changes in goats (%) administered with piroxicam, AA and streptomycin/penicillin (n = 3; Mean ± SEM).

	Group A	Group B	Group C	Group D	Group E	Group F
Immediately after surgery	−2.7	−4.9	0	−3.6	−3.6	−5.1
3 hours post-surgery	−4	0	0	−3.6	−3.6	−6.1
Day 1	2.7	−4.9	0	−3.6	2.4	−13.3
Day 2	2.7	0	−2.1	−3.6	−1.2	−16.3
Day 3	0	1.2	−5.3	0	0	−11.2
Day 4	−4	0	0	0	−1.2	−15.3
Day 5	2.7+	1.2	0	−1.2	2.4	−10.2

Group A – Animals administered with piroxicam at 5 mg/kg (IM) and AA at 100 mg/kg (IV), penicillin 20,000 IU/kg and streptomycin, 10 mg/kg (IM).
Group B – Animals administered with piroxicam at 5 mg/kg (IM) and AA at 200 mg/kg (IV), penicillin 20,000 IU/kg and streptomycin, 10 mg/kg (IM).
Group C – Animals administered with piroxicam at 10 mg/kg (IM) and AA at 100 mg/kg (IV), penicillin 20,000 IU/kg and streptomycin, 10 mg/kg (IM).
Group D – Animals administered with piroxicam at 5 mg/kg (IM) and penicillin 20,000 IU/kg and streptomycin, 10 mg/kg (IM).
Group E – Animals administered with AA at 100 mg/kg (IV), penicillin 20,000 I.U/kg and streptomycin, 10 mg/kg (IM).
Group F (control) – Animals administered with penicillin 20,000 I.U/kg and streptomycin, 10 mg/kg (IM).
–, loss.

surgery across the groups; except Group C, which maintained its baseline weight immediately after surgery and three hours post-surgery. Animals in Group B had the same weight as their baseline, at three hours. On day 1, weight gains of 2.7% were recorded for animals in Group A (days 1, 2 and 4), Group B [day 3 and 5 (1.2%)], Group E [day 1 and 5 (2.7%; Table 3)], while baseline weight was maintained for Group C. However, gradual weight loss was recorded for the control group up to 16% on day 2, while minimal weight losses were recorded in Groups A–E (1.2%; Table 2). At the end of five days, the treated groups recorded weight gains up to 2.7%, while Group F (control) recorded weight loss of about 16% (Table 3).

The RT of the goats remained unchanged immediately after surgery in all the groups. After three hours, the RT still remained unchanged in Groups A and B, decreased in Groups C, D and E; and it increased in Group F. From day 1, the RT did not change significantly ($P < 0.05$) in groups B, C, D and E, but rose in Group A on day 2 and 4. Group F showed a rise in RT on days 2 and 4, which was statistically insignificant ($P < 0.05$; Table 3). There was no correlation between time and RT in all the groups. There was no significant difference between the baseline and experimental values within all the groups, but the RT rose ($P < 0.05$) in the control group (Group F) at the end of the experiment (Table 4), compared to those obtained in all the experimental groups.

It was observed in this study that the treated groups gained LW by 2.7%, while the control animals lost up to 16% weight. The result agrees with the findings of

Table 4. RT responses of goats (°C) administered with different concentrations of piroxicam, AA and streptomycin/penicillin combination (Mean ± SEM, n = 3).

(°C)	Group A	Group B	Group C	Group D	Group E	Group F
Baseline	38 ± 0.52	39 ± 0.15	39 ± 0.20	39 ± 0.44	39 ± 0.50	39 ± 0.26
Immediately after surgery	38 ± 0.52	39 ± 0.15	39 ± 0.20	39 ± 0.44	39 ± 0.50	39 ± 0.26
3 hours after surgery	38 ± 0.56	39 ± 0.15	38 ± 1.2	38 ± 1.1	38 ± 1.1	40 ± 0.58
Day 1	38 ± 0.35	39 ± 0.33	39 ± 0.03	38 ± 0.61	39 ± 0.50	39 ± 0.27
Day 2	39 ± 0.42	38 ± 0.52	39 ± 0.06	38 ± 0.68	39 ± 0.49	40 ± 0.15
Day 3	38 ± 0.38	38 ± 0.72	39 ± 0.17	38 ± 1.1	39 ± 0.59	39 ± 0.15
Day 4	39 ± 0.38	39 ± 0.29	39 ± 0.25	38 ± 0.85	39 ± 0.27	40 ± 0.08
Day 5	38 ± 0.31	38 ± 0.08	38 ± 0.20	38 ± 1.1	39 ± 0.47	39 ± 0.17

Group A – Animals administered with piroxicam at 5 mg/kg (IM) and AA at 100 mg/kg (IV), penicillin 20,000 IU/kg and streptomycin, 10 mg/kg (IM).
Group B – Animals administered with piroxicam at 5 mg/kg (IM) and AA at 200 mg/kg (IV), penicillin 20,000 IU/kg and streptomycin 10 mg/kg (IM).
Group C – Animals administered with piroxicam at 10 mg/kg (IM) and AA at 100 mg/kg (IV), penicillin 20,000 IU/kg and streptomycin, 10 mg/kg (IM).
Group D – Animals administered with piroxicam at 5 mg/kg (IM) and penicillin 20,000 IU/kg and streptomycin, 10 mg/kg (IM).
Group E – Animals administered with AA at 100 mg/kg (IV), penicillin 20,000 I.U/kg and streptomycin, 10 mg/kg (IM).
Group F (control) – Animals administered with penicillin 20,000 I.U/kg and streptomycin, 10 mg/kg (IM).

Table 5. Baseline and post-surgical RT responses of goats administered with different concentrations of piroxicam, AA and streptomycin/penicillin combination (Mean ± SEM, $n = 3$).

	Group A	Group B	Group C	Group D	Group E	Group F
Baseline temperature (C)	38.3 ± 0.52	39.1 ± 0.15	38.5 ± 0.20	38.7 ± 0.44	39.0 ± 0.50	39.2 ± 0.26
Post-surgical temperature (C)	38.3 ± 0.15[a]	38.6 ± 0.14[a]	38.4 ± 0.18[a]	38 ± 0.29[ab]	38.8 ± 0.21[b]	39.4 ± 0.07[a]

[ab]Means with same superscript letters are significantly ($P < 0.05$) different.
Group A – Animals administered with piroxicam at 5 mg/kg (IM) and AA at 100 mg/kg (IV), penicillin 20,000 IU/kg and streptomycin, 10 mg/kg (IM).
Group B – Animals administered with piroxicam at 5 mg/kg (IM) and AA at 200 mg/kg (IV), penicillin 20,000 IU/kg and streptomycin 10 mg/kg (IM).
Group C – Animals administered with piroxicam at 10 mg/kg (IM) and AA at 100 mg/kg (IV), penicillin 20,000 IU/kg and streptomycin, 10 mg/kg (IM).
Group D – Animals administered with piroxicam at 5 mg/kg (IM) and penicillin 20,000 IU/kg and streptomycin, 10 mg/kg (IM).
Group E – Animals administered with AA at 100 mg/kg (IV), penicillin 20,000 I.U/kg and streptomycin, 10 mg/kg (IM).
Group F (control) – Animals administered with penicillin 20,000 I.U/kg and streptomycin, 10 mg/kg (IM).

Johnson (2002) and Landa (2012), who recorded weight loss as a sign of pain, although the degree or percentage weight loss was not evaluated in their studies. Lérias et al (2013) had demonstrated that stressful conditions lead to LW losses in goats. The result of the present study showed that untreated pain causes distress in animals undergoing pain, and ultimately weight loss, which may reduce productivity because the feed intake is also adversely affected (Berry et al. 2001; Lents et al. 2001). Also, LW losses cause reduced fertility and lead to increase vulnerability to diseases and parasites (Lérias et al. 2013).

The elevated RT above normal (T) recorded in the control group in the present study is in agreement with the findings of Sanford et al. (2006) and Landa (2012), who showed that increase in body temperature is indicative of pain. Koknaroglu and Akunal (2013) reported that when the autonomic sympathetic system is stimulated with stress factor, adrenaline is released from the adrenal medulla. Although increased concentration of adrenaline in the circulation has similar effects as that of cortisol, it also increases body temperature (Yurdakoş 2005). A combination of Piroxicam and AA generally decreased RT when its value was elevated (Table 5), and this finding may be due to the involvement of AA as a vitaminergic (inhibitory neurotransmitter) that mitigates the release of adrenocorticotropic hormone from the hypothalamic–pituitary system (Karanth et al. 2000).

4. Conclusion

It is concluded that multi-modal approach to surgical pain management is the best option, and that piroxicam and vitamin C combination is very effective in the management of post-surgical pain, at the dose rate of 10 mg/kg IM and 200 mg/kg IV, respectively. A combination AA and piroxicam ameliorated the effect of stress, improving LW and decreasing body temperature better than either of the agents alone in goats.

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