EFFECT OF GRADED DOSE OF ORAL TRAMADOL ON CORTISOL AND TESTOSTERONE PROFILE OF WEST AFRICAN DWARF BUCK

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Abstracts

The study intended to investigate the effect of long term doses of tramadol on the testosterone and cortisol levels in WAD Bucks. Testosterone and cortisol are one of the major sexually hormone that depicts the reproductive potential of animals. 10 sexually mature WAD bucks were used for the research weighing between 15-18kg. The animals were group into A and B. They both serve as their control [pre-treatment] after which blood was collected from the animal. Tramadol of 50mg and 100 doses were given to animals in group A and B respectively for 21 days daily. Both pre-treatment post treatment serum collected was assayed for testosterone and cortisol using Micro well ELIZA technique. There was no significant difference in the level of cortisol in the bucks with treatment of both 50mg and 100mg. In the testosterone profile, there is significant difference ($p<0.05$) in its level with 100mg but not significant difference in treatment with 50mg dose. From this result it can therefore be deducted that prolonged treatment of algesia with tramadol of 100mg dose should be discourage as its affect the testosterone level which may result into decrease sexual function, a reduction in libido and erectile dysfunction.

Keywords: Tramadol, WAD buck, testosterone, cortisol

Introduction

Tramadol is a synthetic opoid analogue of codeine first synthesized in 1962 by Grunenthal in an attempt to reduce common opoid adverse effects such as respiratory depression (Gruntheal,1976). The use of tramadol as a centrally acting analgesic compound compares to other opoid and non – opoid compound, has been studied in various clinical situation (Matthiesen,1994). It is thought t act by binding to u-opoid receptor and by inhibition of there - uptake of noradrenaline and serotonin (Raffia *et al.*1992,). Tramadol has been indicated for the relief of moderate to severe pain in adult and young animal. It has been clinically evaluated in all surgical discipline; include general, orthopedic, cardiothoracic surgery (5). It has been fund to have linear pharmacokinetic with the therapeutic dosage range. (Kukanich and Papich, 2004).Oral administration of tramadol with food does not significantly affect its rate of or extent of absorption. Therefore tramadol is rapidly completely absorbed orally with regard to food, little or no effect by ruminal content (Martignoni, 2006). It is rapidly distributed in the body and can cross the placental and blood – brain barrier. Very smell and of tramadol and its metabolite are found in milk (Keating, 2006). Tramadol is extensively metabolized after oral administration. The major metabolic pathway appears to be N- and O- demethylation and glucuronidation or sulfation in the liver, only O-desmethyltramadol (M_1) is pharmacologically active. Tramadol and its metabolite are excreted mainly by the kidneys with a cumulative renal excretion (tramadol & its metabolite) of approximately 95%.

Recent research has shown the tramadol exhibit different metabolic rates between species: tramadol is metabolized quickly to inactive metabolite in goat (Ruwwed), horse and dogs (Kucinich and Papich 2004; de souse *et al.,* 2008, Shilo *et al.,* 2008, Giorji *et al.*, 2008).

Patient taking tramadol have been reported to have some gastro intestinal effects, dizziness, headaches and so except that its affect an reproduction parameter in ruminant.(Zoli A,2002) Cortisol is the most well-known glucocorticoid that is secreted by adrenal gland and has very important effects on immune system and body metabolism . Increase in serum cortisol can also influence circulatory system (Arave C.W et al,1978)The study is therefore intend to verity the long term treatment of tramadol on two major sexual / reproductive hormone (testosterone &

cortisol) using varying doses on sexually mature West Africa Dwarf buck.

Materials And Methods

10 sexual matured West African Dwarf (WAD) Bucks weighing between 12 – 15kg fed old libitum with concentrate forage and supply of water. The animals was exposed to necessary clinical maintenance throughout the whole period of the experiment after two weeks of stabilization, the animal were group into group A and B each containing 5 animals.

Pre-treatment and post treatment serum collection and Hormonal Assay

10ml of blood samples were collected through the jugular vein of the WAD bucks by observing all aseptic precaution using sterile needle & syringe. The blood was immediately poured into plain sample bottle. Serum was collected after the clotting and sedimentation of the whole blood. The supernatant which is the serum was decanted to assayed for level of testosterone and cortisol using Microwell enzyme linked immune assay (ELISA) technique using analytical grade reagent (synthron Biorescuk inc. USA (Ekaluo et al. 2010) for the pre-treatment. Treatment of the animal commenced immediately. Group A and B were treated with 50mg / kg and 100mg of tramadol orally respectively for twenty-one day after which the same procedure as for the pre-treatment was repeated for post-treatment for hormonal assays.

Result and Discussion.

Result: The cortisol profile of W.A.D bucks treated with the two doses of tramadol was shown in table1. There were no significant different in the cortisol level of the animals. In table 2, it was shown to present testosterone profile of W.A.D bucks treated with the two doses of tramadol. The treatment group of 50mg/kg was with no significant difference of the p value while the group treated with 100mg/kg show a significant difference at $p<0.05$.

Table1: The cortisol profile of W.A.D bucks treated with the two doses of tramadol.

Group	Pre-treatment(control) (ng/ml) M±SEM	Post-treatment (ng/ml) Mean±SEM
Group A(50mg/kg)	4.19±0.1478	4.04±0.1298
Group B(100mg/kg)	4.85±0.2420	4.65±0.2758

Table2: The testosterone profile of W.A.D bucks treated with the two doses of tramadol.

Dose (mg)	Pre-treatment(control) (ng/ml) M±SEM	Post-treatment (ng/ml) Mean±SEM
Group A(50mg/kg)	5.59±0.152	5.29±0.149
Group B(100mg/kg)	4.70±0.052×	4.44±0.052

Paired t test: × P value significant at $p<0.05$

Discussion

In the result of Table 1, it was observed that the long term utilization of the drug at both dosages causes a decrease in cortisol which is not statistically different. Also testosterone level is not statistically different at the dosage of 50mg/kg. Group B treated with 100mg/kg show a significant different at $p<0.05$.

Testosterone is the most important male reproductive hormone; it is related to reproductive behaviour, spermatogenesis and secondary sexual characteristics (Hafez, 2004). The early reproductive behaviour (mounting) displayed by goats long before the start of puberty has been associated with low testosterone production by the testicles after birth (Skinner, 1970). Testosterone levels are useful in the selection of young sires and to characterise sexual maturity in different breeds (Eloy & Santa Rosa, 1998). Plasma testosterone concentrations are related to age (Silva, 2000), season of the year (Delgadillo and Chemineau, 1992), protein intake (Azevedo Neto, 2005) and drug administration (Mududuli et al., 1979; Delgadillo and Chemineau, 1992). Testosterone is directly involved in the onset of puberty, and consequently in the onset of spermatogenesis (Eloy and Santa Rosa, 1998). Many studies using animal model have confirm the testosterone is important in modulating the central and peripheral regulation of the erectile function and penile thrust. A decrease in serum testosterone has negative impact on the structure and forms of penile tissues and erectile which may ultimately

affect libido (Gahl,2003).

It can therefore be deduced that deducted that prolonged treatment of algesia with tramadol of 100mg/kg dose should be discourage as its affect the testosterone level which may result into decrease sexual function, a reduction in libido and erectile dysfunction.

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