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EFFECTS OF DIURESIS ON UREA INTOXICATION IN SHEEP

(With One Table)

By

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تأثير المدرارات على التسمم باليوريا في الاغنام

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لقد أدى تجريع اليوريا بالفم بجرعة مقدارها (٠,٥) ملجرام للكيلوجرام حي للأغنام الى حالة إحباط وجفاف وتشنجات عضلية ولقد أختفت هذه الأعراض عند حقن دواء الفيروسمايد في الوريد وبجرعة مقدارها ١ ماجرام للكيلوجرام ومحلول الملح الفسيولوجى (٩,%). تم ملاحظة زيادة بدلالة أحصائية في تركيز بلازما الامونيا واليوريا والجليكوز والكريتين مقارنة مع الشاهد. بينما نجح الفيروسمايد ومحلول الملح الفسيولوجى (٩,%) في التسبب في نقصان المتغيرات أعلاه.

SUMMARY

Administration of urea orally at a dose of 0.5 mg/kg body weight to sheep has resulted in depression, dehydration, muscle tremors and convulsions. Those signs were interrupted by intravenous administration of 1mg/kg furosemide and normal saline resulting in fast recovery of animals. Animals dosed with urea showed higher haematocrit values and higher ammonia, urea, glucose and creatinine compared with controls. Treatment with furosamide and fluid therapy has significantly produced lower haematcrit values and ammonia, urea, glucose and ceatinine levels.

Key words: *Sheep, oral, intravenous, urea, furosamide.*

INTRODUCTION

It is now established practice in some parts of the world to upgrade the protein content of low quality roughage by urea treatment (Chenost 2000). Fortunately, large regular supplies of urea are produced

in Saudi Arabia by Saudi Basic Industries Corporation (SABIC) that can be utilized to upgrade nitrogen content of straws (Al-Shami and Al-Sultan, 2006). Although the use of urea by ruminants is usually safe, acute urea poisoning and the death of animals are often cited by veterinarians and farmers. Usually the clinical illness develops quickly and may cause death in a few minutes (Ortolani *et al.*, 2000). Therefore this study is conducted to investigate the value of diuresis in the treatment of urea poisoning in sheep.

MATERIALS and METHODS

A. Animals and housing:

Fifteen Neimi Sheep of 2-3 years old and weighing between 30-35 kg body weight were used in the study. Animals were fed hay and Rhodes grass and water available *aid libitum*.

B. Drug administration:

Animals were alloted into three groups of 5 each. Group 1 was used as untreated control. Group 2 was dosed orally with urea at 0.5mg/kg body weight (Bartley *et al.*, 1976; Edjtehadi *et al.*, 1978). The urea was of analytical reagent grade (Sigma, UK) and was given orally as 10% salution. Group 3 was treated similar to group 2 after 30 minutes, each animals was injected with 1 mg furosemide (Dimazon, Intervet, UK) and fluid therapy as normal saline (0.9% Nacl, Animakare, Aqupharm, UK); both drugs were given intravenously.

C. Clinical Signs and Samples Collection:

Clinical signs were monitored and blood samples (10 ml) were collected into heparinized tubes for preparation of plasma.

D. Assay of different parameters:

Plasma glucose, urea, ammonium and creatinine were determined by Multiple Clinical Chemistry Autoanalyser (Liasys, AMS, Rome, Italy) using commercial diagnostic kits. Haematocrit was determined using microhaematocrit centrifuge.

Statistical analysis:

Values of different parameters were assessed by analysis of variance with application of Duncan's multiple-range tests. $P < 0.05$ was accepted as statistically significant.

RESULTS

A result of the effect of diuresis on urea intoxication in sheep is given in Table 1. The clinical signs in group 2 and 3 included

restlessness, depression, dyspnea, dry muzzle, dehydration and musle tremors. Those signs were interrupted in group 3 by diuretics leading to diuresis, but proceeded further to convulsion in group 2. One animal in group 2 died and 4 animals recovered by third day of experiments. All animals in group 3 recovered on the same day of experiment. Administration of urea resulted in plasma ammonia levels of more than ten-fold increase in group 2 and 3 compared to group 1. All animals dosed with urea showed higher plasma glucose, urea and creatinine levels and higher haematocit values than animals in group 1 ($P < 0.05$). Sheep treated with furosamide and fluid therapy have significantly ($P < 0.05$) lower haematocrit values and ammonia, urea, glucose and creatinine levels.

Table 1: Effeects of diuresis (furosemide) 1mg/kg and normal saline treated intravenously to sheep administrated of urea orally at a dose of 0.5 mg/kg body weight. (n=5 each.)

Variable	Group 1 (Control)	Group 2 (Urea treated)	Group 3 Urea, furosamide and Nacl treated
PCV %	31 ± 2^a	40 ± 3^b	36 ± 2^c
Plasma ammonia (µmol/l)	26.3 ± 3.4^a	314 ± 16^b	205 ± 12^c
Plasma Urea (mmol/l)	2.3 ± 0.31^a	4.6 ± 0.51^b	3.3 ± 0.4^c
Plasmia creatinine (µmol/l)	0.086 ± 0.003^a	0.14 ± 0.005^b	0.115 ± 0.003^c
Glucose (mmol/l)	3.8 ± 0.5^a	7.4 ± 1.9^b	5.1 ± 1.3^c

* a, b, c mean with different superscripit in the column indicates significant difference ($P < 0.05$)

DISCUSSION

The results showed that administration of urea has induced dehydration indicated by clinical signs, increased haematocrit and creatinine concentration. The concentration of plasma ammonia increased many fold, where as that the urea did not exceed twice the normal levels suggesting that ammonia liberated from urea in the rumen is the acutual toxicant (Haliburton and Morgan 1989). It is likely that the liver has reached its physiological limit to synthesis urea (Visek 1979),

resulting in elevated levels of ammonia. Ammonia is a potent irritant to lungs (Kitamura *et al.*, 2003b) and in high concentration causes intense pulmonary edema. Thus sudden migration of fluids to the lungs can cause dehydration, restricted kidney perfusion and smaller urinary excretion of non-protein nitrogen (Roller *et al.*, 1982; Morgan 1997). Similar observation of the urea or ammonia toxicity have been reported in sheep and goat (Edjtehadi *et al.*, 1978; Roller *et al.*, 1982; Ortolani *et al.*, 2000, Kitamura *et al.*, 2003 a,b). High glycemia was also evident in blood of sheep intoxicated with urea. Similar results were obtained in rat (Kitamura *et al.*, 2003b), sheep (Edjtehadi *et al.*, 1978) and cattle (Kitamura *et al.*, 2003a). High ammonia enhances the secretion of glucagon, makes tissue cells refractive to insulin, which increases glucose production and impairs utilization via tricarboxylic acid cycle (Visek 1979; Roller *et al.*, 1982).

Treatment of animal with normal saline and furosamide has resulted in lower plasma creatinine level and haematocrit values. Clinically, the treated animals have showed frequent urination indicating that adequate diuresis has occurred in these animals. It is likely that urinary output may excrete significant toxin leading to decreased levels of blood ammonia and urea (Ortolani *et al.*, 2000). Furthermore, it has been shown that in sheep intoxicated with urea, the surviving group urinated more frequently than the fatal cases in which anuria was evident (Edjtehadi *et al.*, 1978). It would have been better if urea cycle amino acid had been administered to enhance the detoxification of ammonia through urea cycle (Ortolani and Marcondes 1995), a possibilily needs to be tested in sheep.

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