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Butaphosphan and cyanocobalamin treatment of pregnant ewes: Metabolic effects and potential prophylactic effect for pregnancy toxaemia

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ABSTRACT

The effect of administration of butaphosphan and cyanocobalamin on the prophylaxis of pregnancy toxaemia in ewe was investigated. Moreover, the effects of these compounds on body weight gain and biochemical metabolism of pregnant ewe was assessed. A total of 59 pregnant Kıvırcık crossbred ewes were used in this study. Group I (*n*: 15) was administered butaphosphan and cyanocobalamin three times before delivery at 1-week intervals. Group II (*n*: 15) was administered butaphosphan and cyanocobalamin three times before delivery at 3-day intervals. Group III (*n*: 15) was administered 0.9% NaCl three times before delivery at 1-week intervals. Group IV (*n*: 14) was administered 0.9%NaCl three times before delivery at 3-day intervals. Six blood samples were taken from each ewe four times before delivery and two times after delivery. Haematological and biochemical analyses were performed.

The levels of BHB and NEFA in groups administered butaphosphan and cyanocobalamin were noticeably lower but there were no statistically significance. Elevated BHB (>0.8 mmol/L), subclinical pregnancies toxaemia were identified in 56.66% in test groups and 72.41% in control groups in all ewes and this was higher in the ewes bearing multiple pregnancies 71.42 in test groups and 82.35% in control groups. Subclinical pregnancy toxaemia in pregnant ewes with twins or triplets is lower than the levels for the control groups, despite the greater lamb counts and weights of the ewes in test groups.

Based on our results, it was concluded that the butaphosphan and cyanocobalamin combination could be used as an alternative treatment for the prevention of pregnancy toxaemia.

1. Introduction

Toxaemia of pregnancy is a metabolic disorder seen in pregnant ewes, particularly those carrying multiple offspring. The disorder typically occurs during the last 4–6 weeks of pregnancy due to a lack of energy, which increases as the foetus begins to grow (Mobini et al., 2002; Scott,

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2007; Radostits et al., 2007; Schlumbohm and Harmeyer, 2008; Maas and Pearson, 2009; Fthenakis et al., 2012). As the number of offspring is low during the first pregnancy, toxaemia is uncommon and only typically observed only after the 2nd pregnancy period (Radostits et al., 2007).

Pregnancy represents a complex physiological condition involving the integration of a variety of regulatory and organ systems. During this period maternal plasma glucose appears to be a primary energy source for the foetus (Morgante et al., 2010).

The energy intake and glucose turnover rate is approximately 40–100% in the early stages of pregnancy. This rate drops dramatically in the later stages of pregnancy (Schlumbohm and Harmeyer, 2008). In addition, the foetus has a high growth rate in the last 6 weeks of pregnancy, a factor that increases the energy needs for the ewe. A lack of energy, due to various reasons, may occur in ewes pregnant with more than one foetus when energy intake requirements are not met. Consequently, a negative energy balance occurs. This results in a change in the insulin–glucagon ratio during late pregnancy coupled with mobilization of fatty acids and glycerol from energy reserves in adipose tissue used to provide alternative sources of energy for foetal growth (Piccione et al., 2009). If the energy requirement is greater than energy intake, the liver cannot produce enough glucose and, as a result, ketone bodies are formed due to the excessive accumulation of free fatty acids (Mobini et al., 2002). In particular, an increase of beta-hydroxybutyrate (BHB) concentration occurs. This in turn suppresses endogenous glycogen production and increases the development of ketosis (Radostits et al., 2007; Scott, 2007).

Although toxaemia of pregnancy develops similarly to ketosis in dairy cows, the prognosis for ewes suffering toxaemia of pregnancy is less favourable, with a survival rate of approximately 30% with medical treatment (Scott, 2007). Researchers have focused their studies on prophylaxis due to poor response to medical treatment. Treatment of pregnancy toxaemia involves controlling the body condition score in late pregnancy, providing additional concentrated feed, and administering certain drugs (Scott et al., 1998; Herdt and Emery, 1992). The application of butaphosphan and cyanocobalamin in recent years has shown positive results in the prophylaxis of subclinical ketosis in dairy cows (Rollin et al., 2010; Furll et al., 2010). Another study conducted with ewes reported that the administration of butaphosphan and cyanocobalamin during the early postpartum period led to an improvement in metabolic parameters (Pereira et al., 2013).

Cyanocobalamin is a synthetic analogue of vitamin B_{12}. Methylmalonyl-CoA mutase is a mitochondrial enzyme and vitamin B_{12}-dependent gluconeogenetic substrate (Pereira et al., 2013). Butaphosphan is used as an organic source of phosphorus. Phosphorus plays an important role in the intermediate steps of phosphorylation in gluconeogenesis in hepatic carbohydrate metabolism. In addition, phosphorus furthermore plays a key role in energy metabolism with an important role in ATP synthesis (Rollin et al., 2010).

This study examined the combination of butaphosphan and cyanocobalamin, and the effectiveness of this combination in the prophylaxis of pregnancy toxaemia, effects of administration on metabolic parameters, and the prophylactic effect of application in the prepartum period at different time intervals.

2. Material and methods

2.1. Animals and nutrition

The study was approved by Committee of the Animal Experimentation of Uludag University (2011-09/04). The livestock in the study consisted of 59 Kivircik crossbred ewes in at least their 2nd pregnancy. The ewes were obtained from a private sheep farm in Bursa, Turkey. A total of 100 premated ewes were separated. Pregnancy examinations were performed by conducting an ultrasound of the abdominal area, and rectally during the 2nd month postmating. The duration of pregnancy and dates for giving birth were identified for 60 ewes that were both pregnant with twins and had previously given birth at least once. The live weights of these ewes were determined using an electronic scale during the 2nd month of their pregnancies. Planning was performed in accordance with the expected dates for giving birth for ewes at different pregnancy stages, among the ewes with known pregnancy durations.

All ewes were let to graze on pasture during periods when seasonal conditions were appropriate. When the ewes returned to the sheep corral appropriate forage and concentrated feed were provided after the nutritive value of the pasture was taken into consideration. The live weights of the 60 ewes included in this study were determined at the 2nd and 4th months of pregnancy, and at the 1st month of lactation. Averages were calculated. The average live weight of the animals and the twinning status was noted and feed amounts were calculated after considering the minimum nutrient requirements specified in the National Research Council (NRC, 2007). Each ewe was fed 0.3 kg alfalfa, 0.4 kg barley, 1 kg milk replacement, and 0.7 kg dry oats for per day. The average live weights (60.61 ± 1.24 kg on average) were determined at the 2nd month of pregnancy. Forage was increased for each ewe by 14% according to the live weights (average 70.76 ± 1.63 kg) of the animals in the 4th month of pregnancy.

In the postpartum period, the daily nutrient requirements for the ewes were calculated and provided to meet the minimum requirements specified by the National Research Council (NRC, 2007). Following birth, all ewes were set to graze on pasture during appropriate seasonal conditions. When the ewes returned to the sheep corral, forage and concentrated feed were provided after the nutritive value of pasture was taken into consideration. After adjusting for the average live weights, ewes were fed a calculated mixture of barley, alfalfa hay, tomato pomace, potato residue, high moisture corn (22% brix) and oat hay.

2.2. Study design

The ewes were divided into 4 groups of 15 ewes each and grouped according to the number of offspring in the pregnancies and the number of previous pregnancies as follows:

Group I: A combination of 10 mg/kg butaphosphan and 5 μg/kg cyanocobalamin (Catosal inj., 1 cc/10 kg, Bayer®) was administered through a subcutaneous (SC) injection 3 times at 1-week intervals in the last 4th, 3rd and 2nd weeks of the pregnancy for each of the 15 ewes (Test Group-A).

Group II: A combination of 10 mg/kg butaphosphan and 5 μg/kg cyanocobalamin (Catosal inj., 1 cc/10 kg, Bayer®) was administered through a subcutaneous (SC) injection 3 times at 3-day intervals in the last 2nd–3rd weeks of the pregnancy for each of the 15 ewes (Test Group-B).

Group III: 1 cc/10 kg isotonic sodium chloride was administered through a subcutaneous (SC) injection 3 times at 1-week intervals in the last 4th, 3rd and 2nd weeks of pregnancy for each of the 15 ewes (Control Group-A).

Group IV: 1 cc/10 kg isotonic sodium chloride was administered through a subcutaneous (SC) injection 3 times at 3-day intervals in the last 2nd–3rd weeks of the pregnancy for each of the 15 ewes (Control Group-B).

A total of 59 ewes in the 4th month of pregnancy were weighed for ratio arrangement and the dose calculations were determined accordingly. One ewe was removed from the study due to a broken limb.