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RESEARCH ARTICLE

A Randomized Clinical Trial on Comparative Effects of Propylene Glycol, Dexamethasone and Insulin for Treatment of Bovine Ketosis

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ABSTRACT

In the present study, s randomized clinical trials on comparative effects of propylene glycol, dexamethasone and insulin for treatment of bovine ketosis. For this objective, 60 Holstein cows confirmed to have ketosis were studied. Cows were randomly assigned to three equal groups (n=20). Group I: Received 1000 ml of 25% dextrose I/V plus 200 I.U. insulin twice at 48h interval. Group II: Received 1000 ml of 25% dextrose I/V and 0.04 mg /kg of dexamethasone I/M. However, Group III: Received 1000 ml of 25% dextrose I/V and 200 ml of propylene glycol daily. The application was in progress with daily injections for two successive days. Firstly, the clinical signs of ketosis were improved with all treatments with varying degrees. But by the fourth day post treatment, complete recovery was observed in all cases. Concerning plasma glucose, insulin treatment provided a significant ($P<0.05$) improvement in comparison with other groups, but no significant variation was observed in β-hydroxy butyrate. Similarly, ketotic cows treated with insulin showed a significant decrease ($P<0.05$) in the activity of AST and ALT in comparison with dexamethasone and propylene glycol. Cows treated with insulin showed a significant ($P<0.05$) improvement of serum calcium level in comparison with other groups, but non-significant variation in the effect of different treatments on serum phosphorus level. Regarding the effect of different treatments on serum electrolytes, the dexamethasone group caused significant hypokalemia in comparison with other groups. The present results indicate that insulin could provide good results for treatment of cows with ketosis.

INTRODUCTION

Ketosis is an important metabolic disorder in cattle, characterized by the often-excessive release of negative energy reserve constituents, such as non-esterified fatty acids and beta-hydroxybutyrate, in the blood (Constable et al., 2016). Hypoglycemia, or low glucose in the blood, might appear, although clinical ketosis doesn't necessarily include hypoglycemia (Cainzos et al., 2022; Zhang and Ametaj, 2020). It leads to several problems, such as a decrease in milk yield, increased occurrence of udder diseases, and ketone bodies in the urine (Baird, 1982). Despite various methods to prevent clinical ketosis, the treatment of cattle that show ketosis is still of great importance (Lei and Simões, 2021).

Lipolysis is typical of very sharp transitions associated with ketosis (Guliński, 2021). Cows at the beginning of lactation in negative energy balance mobilize triglycerides intensely, which leads to an increase in plasma non-esterified fatty acids concentration (Rico and Barrientos-Blanco, 2024). That's why NEFA checking is a useful method for diagnosing actual energetic status. The high level of beta-hydroxybutyric acid is a result of acid-balance metabolism deficit and development of metabolic acidosis (Tufani et al., 2011). Although the degree of changes may vary, cattle in a negative energetic status present a common characteristic: increased excretion of ketone bodies in urine, milk, and/or blood (Constable et al., 2016). In cows, the level of beta-hydroxybutyrate, the most common ketone body, is rising. High levels of BHBA are also due to increased glucose demand because the glucose necessary for the neural cells mainly comes from oxidative glucose metabolism. Increased glucagon concentration is responsible for lipolysis and mobilization of NEFA in the adipose tissue. The glycerin required for gluconeogenesis in the liver is a byproduct of lipolysis. The cows need additional energy substrates and moderate glucose demand to prevent a lack of glucose. However, our results showed that cows with ketosis had decreased glucose concentration (Constable et al., 2016).

High incidence of clinical and subclinical ketosis causes economic loss to the dairy fanners due to loss of milk production as wel1 as sharp drop in the SNF content of milk and f1iilure of affected animals to return to normal production after recovery (Constable et al., 2016). Therefore, treatment is essential to restore production and to save animal life (Marzok and El-khodery, 2017).

Several treatment trials have been approached for bovine ketosis (Jeong et al., 2018). Treatments varied in the magnitude of decreasing blood BHB concentrations in hyperketonemic postpartum cows, with the greatest decline after treatment with a combination of intravenous glucose and oral propylene glycol (Mann et al., 2017).

Insulin was found to be beneficial for ketosis treatment in animals with blood glucose < 2.2 mmol/L at ketosis (Gordon et al., 2017). However, there is no available information about the comparison between insulin and other treatment regimens for bovine ketosis. Hence, in this investigation, A randomized clinical trial has been applied assess comparative effect of propylene glycol, dexamethasone and insulin for treatment of bovine ketosis.

MATERIALS AND METHODS

Cows

Sixty-eight Holstein cows confirmed to have ketosis were studied in Northern and Middle regions of Egypt. Diagnosis was based on clinical findings, serum biochemistry. The present study has been approved by the University of King Faisal (KFU 1511).

Hematological examination

Blood samples were obtained from each cow with ketosis (three samples). One sample for hematological examination was collected into a tube with anticoagulant, while the second sample was collected to obtain serum. Hematological investigation was carried out by use of cell counter (MS 9, Franc). The third sample was collected on sodium fluoride for determination of blood glucose levels.

Biochemical examinations

Blood glucose, β-hydroxy butyrate, serum electrolytes (Potassium and sodium) and macro-element (calcium and phosphorus) were measured using the spectrophotometry (test kits: Tecodiagnostics, USA) according to the standard technique. AST and ALT were also measured spectrophotometrically according to standard techniques (SEppim, France).

Treatment trials

The ketotic cows were allocated randomly into three equal groups (20 each). Group I: Received 1000 ml of 25% dextrose (SEDICO, Co. Egypt) I/V plus 200 I.U. insulin (SEDICO, Co. Egypt) twice at 48h interval. Group II: Received 1000 ml of 25% dextrose I/V and 0.04 mg /kg of dexamethasone (EIPICO, Co. Egypt) I/M. However, Group III: Received 1000 ml of 25% dextrose I/V and 200ml propylene glycol (Ketol, Intervet UK Ltd, Egypt) daily. The application was in progress with daily injection for two successive days.

Statistical analysis

For statistical analysis, a commercial software program was used (STATA ver. 18, USA). To ensure that the cows' groups were homogenous, Kruskal Walis test was used. Furthermore, repeated measure ANOVA was used to assess the effectiveness of time and treatments. If the result is positive, further One-way ANOVA was used before and after treatment. At $P< 0.05$ the result was considered significant.

RESULTS

Firstly, the clinical signs of ketosis were improved with all treatments with varying degrees. But by the fourth day post-treatment, complete recovery was observed in all cases. The effect of treatments on the biochemical parameters revealed improvement in all parameters with time, but there was a significant difference among the used drugs. Concerning plasma glucose, insulin treatment provided a significant ($P < 0.05$) improvement in comparison with other groups (Figure 1), but no significant variation was observed in β-hydroxy butyrate (Figure 2).

Similarly, ketotic cows treated with insulin showed a significant decrease ($P < 0.05$) in the activity of AST and ALT in comparison with dexamethasone and propylene glycol (Figure 3-4).

Cows treated with insulin showed a significant ($P < 0.05$) improvement of serum calcium level in comparison with other groups (Figure 5), but non-significant variation in the effect of different treatments on serum phosphorus level (Figure 6).

Regarding the effect of different treatments on serum electrolytes, the dexamethasone group caused significant hypokalemia in comparison with other groups (Figure 7). However, other parameters did not show significant variation among treatments.

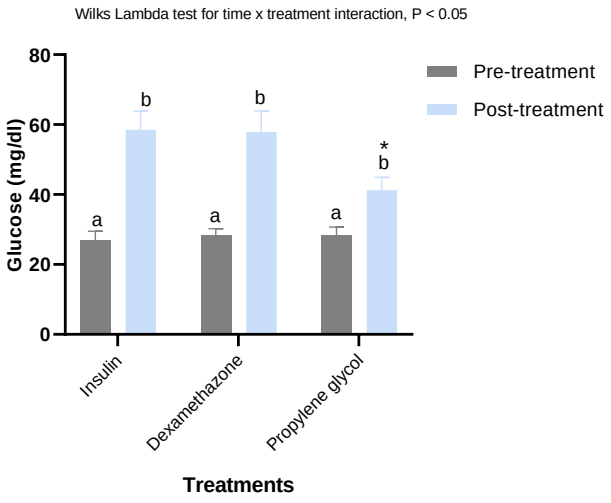

Figure 1. Comparative effects of glycol propylene, dexamethasone and insulin on glucose (mg/dl) in cows with ketosis. a,b: Significance between pre-treatment and post-treatment in the same group at $p < 0.05$. *: Significant differences in post-treatment values among treatment groups at $p < 0.05$.

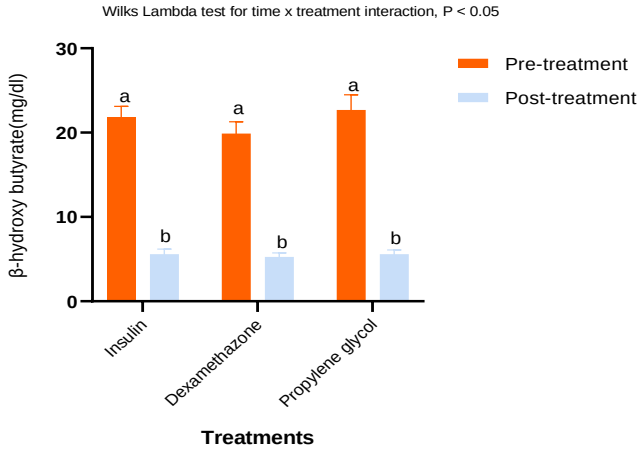

Figure 2. Comparative effects of propylene glycol, dexamethasone and insulin on β-hydroxy butyrate (mg/dl) in cows with ketosis. a,b: Significance between pre-treatment and post-treatment in the same group at p < 0.05. *: Significant differences in post-treatment values among treatment groups at p < 0.05.

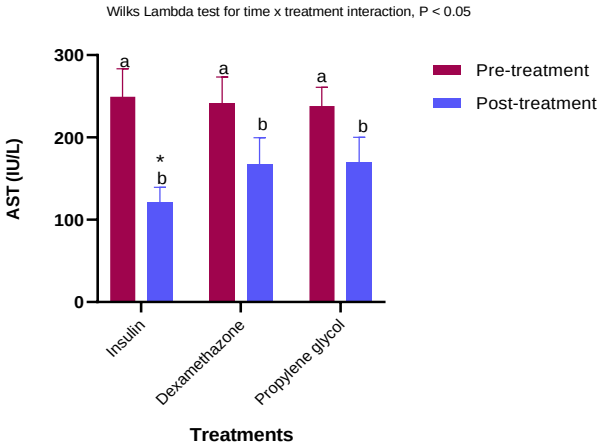

Figure 3. Comparative effects of propylene glycol, dexamethasone and insulin on AST(IU/L) in cows with ketosis. a,b: Significance between pre-treatment and post-treatment in the same group at p < 0.05. *: Significant differences in post-treatment values among treatment groups at p < 0.05.

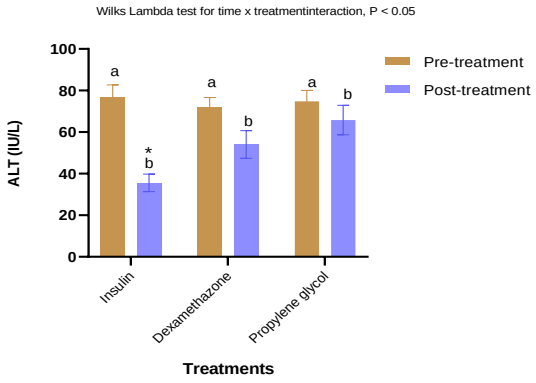

Figure 4. Comparative effects of propylene glycol, dexamethasone and insulin on ALT (IU/L) in cows with ketosis. a,b: Significance between pre-treatment and post-treatment in the same group at p < 0.05. *: Significant differences in post-treatment values among treatment groups at p < 0.05

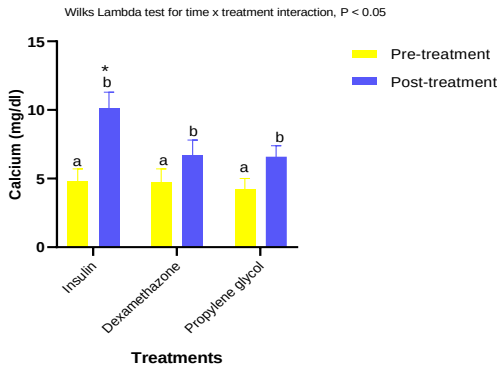

Figure 5. Comparative effects of propylene glycol, dexamethasone and insulin on serum calcium (mg/dl) in cows with ketosis. a,b: Significance between pre-treatment and post-treatment in the same group at p < 0.05. *: Significant differences in post-treatment values among treatment groups at p < 0.05

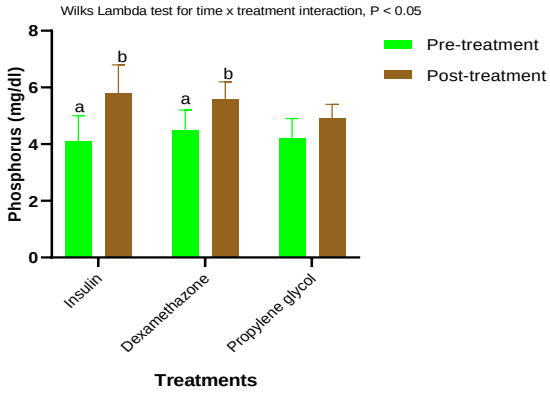

Figure 6. Comparative effects of propylene glycol, dexamethasone and insulin on serum phosphorus (mg/dl) in cows with ketosis. a,b: Significance between pre-treatment and post-treatment in the same group at p < 0.05. *: Significant differences in post-treatment values among treatment groups at p < 0.05

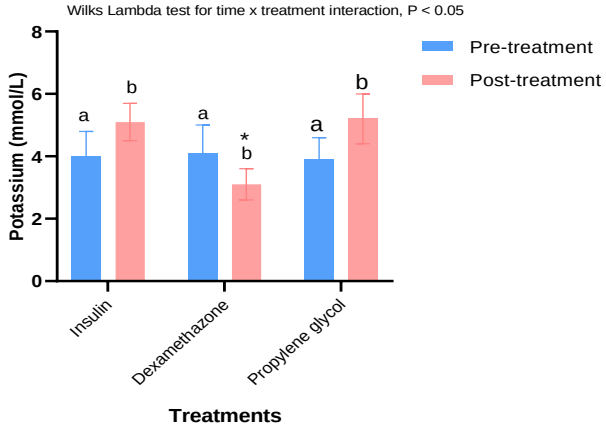

Figure 7. Comparative effects of propylene glycol, dexamethasone and insulin on serum potassium (mmol/L) in cows with ketosis. a,b: Significance between pre-treatment and post-treatment in the same group at p < 0.05. *: Significant differences in post-treatment values among treatment groups at p < 0.05

DISCUSSION

Ketosis is a major metabolic disorder affecting dairy cows with consequent high economic losses. Measurement of blood BHB values in serum or plasma is still recognized by several studies as the gold standard test for diagnosing ketosis (Lei and Simões, 2021). In the present study, the comparative effect of three treatments on the biochemical variables were assessed in a randomized clinical trial.

Clinically, all treatments provided good results, and the complete recovery was observed on the fourth day post-treatment. These clinical findings were supported by blood analysis. However, it has been observed that highest blood glucose increment across time points and insulin by day 7 post treatment (Chirivi et al., 2023).

In the current investigation, insulin provided the best finding in comparison with dexamethasone and propylene glycol. It was suggested that insulin is never given as the sole treatment of ketosis, because of the risk of hypoglycemia (Gordon et al., 2013). There were three studies that used insulin as an adjunct therapy in which the added benefits of insulin could be examined(Hayirli, 2006; Robertson, 1966; Seifi et al., 2007). Results from the Robertson study indicated that the addition of insulin increased cure rate and milk production compared with treatment with glucocorticoids alone (Robertson, 1966).

Cows treated with insulin had significantly lower blood BHB concentrations and significantly higher glucose and insulin concentrations at day 6 after enrollment than cows treated with dextrose alone (Sakai et al., 1993). However, this study had a short follow-up period and did not look at any economically important outcomes, such as milk production and culling. On the contrary, insulin had no effect on blood ketone body concentrations 1 or 2 weeks after treatment or on the likelihood of cure of ketosis based on blood BHB concentrations (Gordon et al., 2012).

Regarding the effect of treatment on minerals in the present study, cows treated with insulin showed rapid significant improvement in the mineral levels (calcium and phosphorus). Contradictory, treatments did not lead to differences in plasma mineral concentrations (Mann et al., 2017).

Regarding the effect of propylene glycol, much of the work carried out with propylene glycol and ketosis involved prevention of ketosis (Nielsen and Ingvartsen, 2000). It has been shown that there is a significant increase in insulin by 15 minutes after administration of propylene glycol, and insulin remains increased for 2 hours or more after drenching (Studer et al., 1993).

In the present study, combination therapy was used, thus glucose plus insulin, or dexamethasone, or propylene glycol was used. Many studies of ketosis treatment have used combinations of therapies. Many of these studies have shown that animals treated with more than 1 product have better outcomes than animals treated with only 1 treatment (Carrier et al., 2011).

Regarding dexamethasone treatment, it provided less efficacy in comparison with insulin and propylene glycol. It was reported that corticosteroid alone was less efficacious than treatment with glucose and a corticosteroid for treatment of bovine ketosis (Shpigel et al., 1996). In our study, dexamethasone induced hypokalemia, and this may not support excessive use of dexamethasone for treatment. This suggestion is supported by the previous study, which conclude less efficacy of dexamethasone for treatment of bovine ketosis (Tatone et al., 2016).

CONCLUSION

The results of the present investigation conclude that ketosis is a major obstacle for production in dairy cows, and rapid intervention is mandatory to restore the energy balance. Insulin treatment can provide useful results for treatment of ketosis in lactating dairy cows.

Authors' Contributions

Conceptualization: M. M., K. A.; Methodology: M.M., K. A.; Analysis: M. K.; Drafting: K.A., M.K.; Review: M.M.; Supervision: M.M

Conflicts of Interest: "The authors declare no conflict of interest.

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