Biochemical Alternation Caused by Bovine Respiratory Disease and Ceftiofur

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Abstract

The most prevalent and dangerous disease in herds that raise calves is bovine respiratory disease (BRD). In the US, the antibiotic ceftiofur, a third-generation cephalosporin, is authorized for use in cattle. The purpose of this study was to investigate the biochemical changes caused by the BRD and the effectiveness of ceftiofur.

On a dairy farm, thirty Holstein calves were split up into three groups. Group I served as a constructively critical group. Group II consisted of healthy animals that received a single subcutaneous ear injection of ceftiofur (2 mg/kg B.W.) Group III, clinically investigated to be suffering from BRD, was given ceftiofur with the same dose and administration route as group II. After taking drugs, all groups underwent clinical evaluations for sickness scores on days 0, 7, and 14.

Biochemical examination revealed a large rise in globulin and a significant decrease in total proteins and albumin ($P<0.05$) on day 0 and 7th where globulin levels increased significantly ($P<0.05$) on day 14th, elevated liver enzyme levels and renal function tests in the diseased treated group. In comparison to the control group, the biochemical values in the healthy treatment group did not alter significantly. In conclusion the research results showed that a number of biochemical markers were significantly impacted by respiratory disorders in calves. Because ceftiofur had a high rate of success, minimal negative effects on clinical indicators, and an appropriate dose and administration schedule, it may be the prescribed medication for BRD.

Keywords: Bovine respiratory disease, effectiveness, Ceftiofur, Calves, biochemical marks.

Introduction

Bovine respiratory disease (BRD) is a disease that affects the respiratory tracts of dairy and beef cattle. Roughly one in five calf deaths was attributed to BRD, making it a significant cause of calf mortality. (***USDA, 2018***).

In order to prevent a detrimental impact on calf productivity, BRD diagnosis is essential in calves. For instance, in preweaning calves, a temporal correlation was found between lung consolidation and decreased average daily growth (***Rhodes et al., 2021***)

Preweaning BRD were linked to an increased risk of decreased mean daily gain, mortality, not finishing the first lactation, and producing less milk during the first lactation in dairy calves compared to their healthy counterparts. Thus, early detection of BRD in calves at risk may help to mitigate the disease's impact on calf productivity (***Buczinski et al., 2021***).

In calves affected by BRD, serum biochemical abnormalities were common and appeared to be rather consistent modifications in reaction to inflammation, leading to significant differences in protein profiles (***Mahmoud et al., 2022***).

The third-generation cephalosporin ceftiofur is only administered to animals. It works well against bacteria of both the Grame positive and Grame negative varieties, such as *Escherichia coli, Pasteurella multocida, Haemophilus somnus*, and *Pasteurella haemolytica* **(*Vilos et al., 2014*).**

This antibiotic has received approval on a global scale to treat infectious infections in horses, pigs, sheep, and goats, as well as for the management of cattle infections of the extremities and metritis (***Hornish et al., 2002***).

Ceftiofur is a β-lactam antibiotic, which means that it binds to penicillin-binding proteins to impede the manufacture of cell walls and prevent the synthesis of peptidoglycan, which, in an isotonic environment, leads to cell lysis **(*Lisignoli et al., 2001*).**

The goal of this research was to assess the biochemical changes in BRD-affected calves as well as the efficacy of ceftiofur.

Material and method

The investigation made use of a range of chemicals and laboratory supplies to carry out tests and analyses.

Drug:

Ceftiofur crystalline free acid (marketed under the brand name Excede®) was procured from Zoites, company, in the form of a sterile suspension. One milliliter contains 200 milligrams of ceftiofur crystalline free acid. A single 2 mg/kg B.W. dose of ceftiofur was subcutaneously injected into the posterior side of the middle third of the ear **(*Salmon et al., 1996*).**

The use of animals in experiments: Investigations were conducted on thirty Holstein calves, ages 45 to 60 days, weighing 39 to 60 kg on average. On a private dairy farm in the Egyptian governorate of Damietta, the study was conducted. When calves with BRD were visually assessed, their symptoms, including fever, discharge from the nose and eyes, respiratory distress, coughing, depression, and inappetence, were reported and scored **(*McGuirk, 2008*).** The three groups of ten calves each comprised the calves that were part of the study. Serving as the healthy, untreated control group was the first group. Ceftiofur was given subcutaneously to the second group of healthy-treated calves at a dosage of 2 mg per kilogram of body weight. The clinically diseased BRD calves in the third group received the same dosage and method of ceftiofur treatment as the second group. All animals were housed in identical conditions with regards to feeding, management, and hygiene, irrespective of the group to which they belonged. All of the calves underwent clinical evaluations using the procedures outlined by (***Radostits et al., 2000*).**

This study was permitted by the Ethics Committee in Faculty of Veterinary Medicine at Suez Canal University (Code no. 2019535)

Three blood samples were collected on day 0, 7th and 14th by use of a jugular vein puncture from every calf (***Radostits et al., 2000***). The blood sample was drawn without the use of an anticoagulant, allowed to be clotted at room temperature for 20 minutes, and then centrifuged for 10 minutes at 3,000 rpm. The clear, non-hemolyzed serum samples were then separated and kept for biochemical analysis at -20°C **(*Stoffregen et al., 1997*).**

Biochemical analysis

A spectrophotometric (Spectronic 20 D, Milton Roy Company) analysis of serum total proteins was conducted using the method outlined by (***Pagana and Pagana, 2010***). Calorimetric determination of albumin was performed using the dye-binding technique with bromocresol in accordance with (***Fischbach and Dunning, 2009***). The variations between total protein and albumin were used to calculate serum globulin, according to (***Chernecky and Berger, 2008***). Additionally, serum samples were utilized to measure alkaline phosphatase (ALP), aspartate transaminase (AST), and alanine aminotransferase (ALT) using specialized kits in accordance with the protocol that was described by (***Pagana and Pagana, 2010***) respectively. Using specialized kits (Diamond), the concentrations of serum urea and creatinine were also measured spectrophotometrically in accordance with the protocol outlined by (***Peake and Whiting, 2006***) respectively.

Statistical Analysis

Statistical package for social science (SPSS) was used for statistically

analyzing of the obtained data recording the mean ± SE variance was analyzed by one way (ANOVA) for analyzing total variation. Duncan test was used for determining significant. probability levels of less than 0.05 were considered statistical significance. Different letters were significantly different, and the highest value was represented with the letter a.

Results

The research results revealed no appreciable differences in the total protein of the healthy treated and control groups; however, at zero days, the diseased treated group's total protein significantly decreased ($p<0.05$) in comparison to the healthy treated and control groups. while on day 7th and14th showed no significant changes between the groups post treatment. The serum albumin level revealed a marked decline in the diseased treated group compared to the healthy treated and control group at day 0 and 7th while at day 14 a significant elevation in the healthy and diseased treated group compared to control group. The serum globulin showed anon significant change on 0 and 7th days, the diseased treated group at day 14th showed a significant release compared to the other groups. After treatment, the diseased group's bilirubin level significantly increased in comparison to the other groups. (table 1).

Compared to the healthy treated and control groups, there was a notable rise in the ALT, AST, and ALP levels in the diseased treated group on days 0, 7, and 14. (table 1).

In comparison to the healthy treated and control groups, the disease-treated group's urea and creatinine levels significantly increased. (Figures 1 & 2).

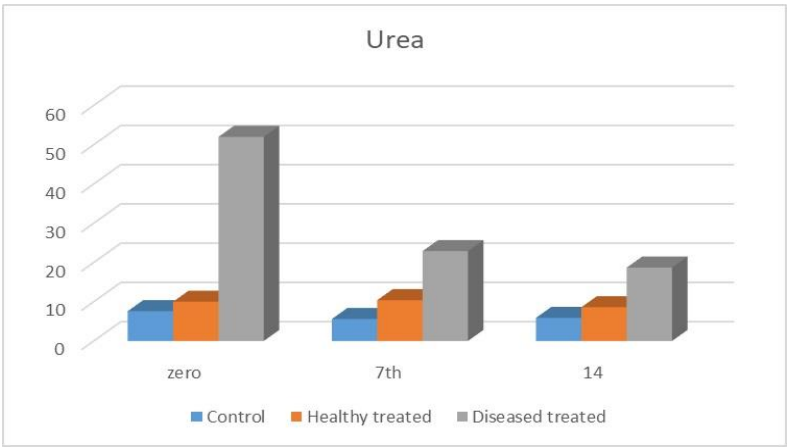

Figure (1) effect of ceftiofur on urea

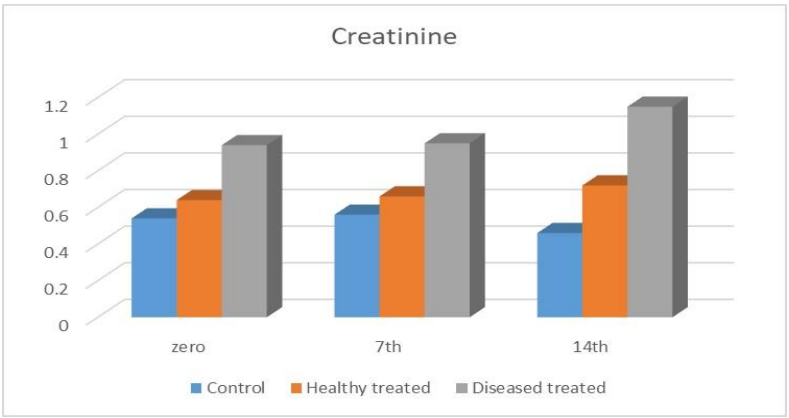

Figure (2) effect of ceftiofur on creatinine.

Table 1. *Some biochemical parameters of control and ceftiofur treated calves.*

parameter	groups	Zero-day	7th	14th
Total protein (g/dl)	Control	5.46±0.29[a]	5.14±0.22[a]	5.23 ±0.23[a]
	Healthy treat.	5.64±0.22[a]	5.14±0.26[a]	5.37±0.22[a]
	Diseased treat.	4.71±0.27[b]	4.77±0.31[a]	5.66±0.39[a]
Albumin (g/dl)	Control	3.58±0.18[a]	3.32±0.18[a]	3.24±0.13[b]
	Healthy treat.	3.73±0.16[a]	3.28±0.16[a]	3.42±0.12[a]
	Diseased treat.	3.15±0.12[b]	3.17±0.19[b]	3.46±0.14[a]
Globulin (g/dl)	Control	1.88±0.07[a]	1.82±0.09[a]	1.99±0.07[b]
	Healthy treat.	1.91±0.07[a]	1.86±0.06[a]	1.95±0.06[b]
	Diseased treat.	1.56±0.11[a]	1.60±0.09[a]	2.20±0.06[a]
Bilirubin (g/dl)	Control	0.02±0.00[b]	0.03±0.00[b]	0.03±0.00[b]
	Healthy treat.	0.04±0.00[b]	0.03±0.00[b]	0.02±0.00[b]
	Diseased treat.	0.24±0.04[a]	0.24±0.02[a]	0.13±0.01[a]
ALT (IU/L)	Control	5.20±0.38[b]	5.70±0.51[b]	4.10±0.34[c]
	Healthy treat.	6.00±0.33[b]	5.90±0.43[b]	5.90±0.37[b]
	Diseased treat.	12.00±1.26[a]	11.00±2.50[a]	8.30±0.65[a]
AST (U/L)	Control	33.20±1.92[b]	31.50±2.37[b]	32.90±0.55[c]
	Healthy treat.	39.20±2.32[b]	33.40±1.66[b]	42.50±1.80[b]
	Diseased treat.	71.20±7.18[a]	92.40±14.68[a]	64.30±4.32[a]
ALP (U/L)	Control	286.90±22.08[b]	298.80±14.60[b]	233.60±1.14[b]
	Healthy treat.	284.80±21.50[b]	310.50±19.70[b]	286.80±21.74[b]
	Diseased treat.	463.70±71.03[a]	584.10±106.69[a]	653.10±47.77[a]

Discussion

The development of bovine respiratory disease (BRD) is a complex, multidimensional sickness that is influenced by the interplay of infectious etiological organisms (viruses and bacteria), environmental stresses, and the animal's immune system (***Panciera and confer, 2010***).

The management and treatment of BRD in cattle depend on the use of

antimicrobials; typical antimicrobial medications that are licensed for use in the US to treat BRD include ceftiofur (***Apley, 2015***).

The study result showed alternation in the serum biochemical analysis in BRD-affected calves This agreed to a study reported by (***El-Seidy et al., 2003; Šoltésová et al., 2015***) who noted that variations in the blood biochemistry in calves affected by BRD were likewise frequent, could show fairly predictable changes in response to inflammation, and resulted in a notable variation in the protein composition.

The previous published studies by (***Novert, 2004; Metwally et al., 2017***) showed that hyperpyrexia and metastatic infection over the course of BRD were the causes of the changes in the biochemical parameters (liver enzyme activity level, urea, and creatinine level) in the respiratory disease.

The results of the study indicated that there was a significant drop in serum albumin and total proteins in the BRD-affected calves serum proteins analysis. These results agree with (***Kalaeva et al., 2019***) who reported that Infections, inflammatory, malignant, cicatricial digestion, liver, renal, and intestinal function disorders, as well as malnourishment, are associated with hypoproteinemia in ruminants.

Also, a significant change in serum albumin and increase globulin level agreed with the previous results of (***Kumar et al., 2018; Anwar et al., 2019***).

The hypoproteinemia, hypoalbuminemia, and hyperglobulinemia that are reported are typically caused by the afflicted animals' anorexia and the liver's inability to produce enough protein. Moreover, it could be because of bacteria and their toxins, which make blood capillaries more permeable and allow plasma proteins to escape from tissues, increasing the osmatic pressure of proteins in tissue fluids while decreasing it in blood (***Attia et al., 2016***).

Additionally, regarded as a negative acute phase protein, albumin's value regularly and noticeably decreases during inflammation (***Georgieva et al., 2011***).

The main protein in the negative acute phase is serum albumin. According to reports, 30–40% of the hepatic protein anabolic capacity is required during the acute phase response to produce positive acute phase proteins. As a result, other protein production must be reduced, which leads to hypoalbuminemia (***Šoltésová et al., 2015; Anwar et al., 2019***).

The potential cause of the observed rise in globulin levels in BRD-affected calves in our investigation could be attributed to the immune system being stimulated by pathogenic organisms (***Anwar et al., 2019; Ramadan et al., 2019***).

Significantly elevated bilirubin levels are consistent with (***Marcato et al., 2021; Assenat et al., 2004***) who illustrated that Lower liver

clearance of secretory enzymes in response to injury to liver cells is linked to greater bilirubin concentrations. In cattle, particularly dairy cows, bilirubin is frequently used as an indicator of liver health (***Bertoni et al., 2008***).

As in earlier research, BRD-affected calves showed a significant ($P<0.05$) rise in ALT and AST when compared to healthy calves. There was also a significant elevation in AST (aminotransferase), ALP (alkaline phosphatase aspartate), and alanine aminotransferase (***Almujalli et al., 2015; Metwally et al., 2017; Kumar et al., 2018*)**.

Higher activity of AST in calves with BRD probably resulted from increased respiratory rate and muscle work during prolonged duration or severe cases of respiratory disease (***Šoltésová et al., 2015***). Also, the significant elevation in ALT, AST levels could be attributed to dysfunction of liver due to hepatic degenerative and necrotic changes caused by bacterial infection and toxins (***Aytekin et al., 2011***).

Significant increase in the urea and creatinine agrees with the previous studies of **(*Almujalli et al., 2015; Metwally et al., 2017 and Kumar et al., 2018; Anwar et al., 2019*).**

The elevation in serum urea concentration of BRD calves could be accounted for by the body's faster protein catabolism and could be a reaction to an illness, but the rise in serum creatinine due to kidney dysfunction after infection **(*Constable et al., 2017; Anwar et al., 2019***).

The study findings revealed no appreciable shift in ceftiofur healthy treated group in the total protein, serum albumin, globulin, the ALT, AST, ALP, urea and creatinine this agree with (***Vilos et al., 2014*)** who reported that The parameters associated with liver function (albumin, globulins, bilirubin, and hepatic enzymes: alkaline phosphatase, aspartate aminotransferase, and alanine aminotransferase) did not show significant changes in both toxicological experiments, demonstrating that ceftiofur microparticles do not affect liver function at the tested doses. Creatinine and urea levels remained unchanged in all study groups, indicating that microparticles and their breakdown products do not cause renal alterations at therapeutic or high doses.

Conclusion

One of the diseases that affects feedlot cattle calves the most economically is BRD. Change the impacted calves biochemical characteristics to create a prediction tool for the wellbeing of BRD-affected calves. Ceftiofur, an antibacterial medication, has no harmful effects on biochemical parameters and can offset the financial loss incurred by BRD-affected calves.

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التغيرات الكيميائية الحيوي الناتجه عن أمراض الجهاز التنفسي والسفتيفور

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الملخص العربي

يعتبر مرض الجهاز التنفسي البقري هو المرض الأكثر انتشارًا وخطورة في قطعان تربية العجول. تمت الموافقة على استخدام السفتيفور ، وهو مضاد حيوي من الجيل الثالث للسيفالوسبورين، في الماشية في الولايات المتحدة. أجريت هذه الدراسة لمعرفة التناوب الكيميائي الحيوي لمرض الجهاز التنفسي وفعالية السفتيفور.

تم تقسيم ثلاثين عجلاً من عجل الهولشتاين في مزرعة ألبان إلى ثلاث مجموعات. تم استخدام المجموعة الأولى كمجموعة سلبية صحية. المجموعة الثانية: ضمت حيوانات سليمة تم حقنها السفتيفور(2 ملغم/كغم من وزن الجسم) تحت الجلد في الأذن كجرعة واحدة. المجموعة الثالثة، التي تم فحصها سريرياً على أنها تعاني من مرض الجهاز التنفسي ، تم إعطاؤها السفتيفور بنفس الجرعة وطريقة التناول مثل المجموعة الثانية. تم تقييم جميع المجموعات سريريًا في اليوم الصفر والسابع والرابع عشر بعد تناول الدواء لقياس درجة المرض، وأظهر التحليل الكيميائي الحيوي انخفاضًا ملحوظًا في إجمالي البروتينات والألبومين وزيادة ملحوظة في الجلوبيولين في اليوم الصفر واليوم السابع مع انخفاض معنوي زيادة في الجلوبيولين في اليوم الرابع عشر وزيادة في نشاط أنزيمات الكبد واختبار وظائف الكلى في المجموعة المريضة المعالجة. أظهرت المجموعة المعالجة صحياً تغيراً غير معنوي في المعايير الكيموحيوية مقارنة بالمجموعة الضابطة. وفي الختام أظهرت نتائج الدراسة أن عدداً من المؤشرات البيوكيميائية تأثرت معنوياً باضطرابات الجهاز التنفسي في العجول. نظرًا لأن السفتيفور يتمتع بمعدل نجاح مرتفع، وتأثيرات سلبية قليلة على المؤشرات السريرية، و مناسب للجرعة والتناول، فقد يكون هو الدواء المعالج لمرض الجهاز التنفسي.