Case report: serum cardiac troponin I concentration in three calves with doxycycline overdose

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SUMMARY

Doxycycline is used to treat or to prevent respiratory infections in calves. Doxycycline can be easily administered to calves in milk or milk replacers; under farm conditions, therefore, overdose may occur in calves. A male, one-month-old Simmental calf was brought to Firat University Veterinary Animal Teaching Hospital because he had anorexia and lethargy. Clinical examination revealed a swollen tongue and tongue paralysis. Doxycycline hyclate, total amount 1500 mg (which is 6.5 times the recommended dose of 5 mg/kg BW), had been administered orally to the calf 3 days previously to treat diarrhea. Based on the history and the results of clinical examination the calf was diagnosed with doxycycline overdose. The case history revealed that two calves on the same farm were also suffering from doxycycline overdose and another calf had died suddenly after doxycycline administration. Increased serum cardiac troponin I (cTnI) concentration of the three calves was determined with a human commercial cTnI assay. The first calf progressively deteriorated and died on day 9 despite decreasing serum cTnI concentration. The serum cTnI concentration of the other two calves returned to physiological levels. In this report, calves with doxycycline overdose had increased serum concentrations of cTnI. Further studies are required to detect whether temporary myocardial damage occurs in doxycycline-overdosed calves.

Keywords : Antibiotic, calf, doxycycline, myocarditis, troponin.

RÉSUMÉ

Cas clinique : concentration sérique de troponine I cardiaque chez trois veaux lors de surdosage par la doxycycline

La doxycycline est utilisée pour traiter ou prévenir les infections respiratoires chez les veaux. Elle peut être administrée dans le lait ou les aliments d’alaitement, un surdosage peut donc se produire chez les veaux dans les conditions d’élevage. Un veau mâle Simmental âgé d’un mois a été amené à l’Université vétérinaire de Firat, parce qu’il souffrait d’anorexie et de léthargie. L’examen clinique a révélé un gonflement et une paralysie de la langue. De la doxycycline sous forme d’hyclate avait été administrée par voie orale au veau pendant 3 jours pour traiter une diarrhée : quantité totale de 1500 mg (soit 6.5 fois la dose recommandée). Les antécédents et les résultats de l’étude clinique du le veau ont permis le diagnostic d’un surdosage de doxycycline. Une enquête dans l’élevage a révélé que deux veaux de la même ferme souffraient également de surdosage et qu’un autre veau était mort subitement après surdosage de doxycycline. Une augmentation de la concentration sérique en troponine I cardiaque (cTnI) a été mesurée chez les trois veaux à l’aide d’un test cTnI commercial humain. L’état de santé du premier veau s’est progressivement détérioré et il est mort le 9e jour malgré une diminution de concentration sérique de cTnI. Les concentrations sériques en cTnI des deux autres veaux sont revenues à des niveaux physiologiques. Des études complémentaires sont nécessaires pour déterminer si des lésions myocardiques temporaires surviennent chez les veaux lors de surdosage par la doxycycline.

Mots-clés : veau, doxycycline, surdosage, myocardite, troponine.

Introduction

Doxycycline is a second-generation semisynthetic tetracycline and has better pharmacological properties than conventional tetracyclines because of excellent penetration into tissues. Doxycycline is used to treat or to prevent respiratory infections in calves [14]. Doxycycline can be easily administered to calves in milk or milk replacers; under farm conditions, therefore, overdose may occur in calves. Cases of accidental poisoning in calves after oral intake of high doses of doxycycline have been reported in Belgium, Israel, Canada, and Netherlands [2,11,18,19]. The major problems in doxycycline-overdosed calves include myopathies, and clinical findings ranging from anorexia to tongue paralysis, and sudden death, have been observed [2,3,5]. Although cardiac effects of doxycycline overdosing in calves were investigated in experimentally induced and field occurring cases, to the authors’ knowledge blood cardiac troponin I (cTnI) concentration in doxycycline-overdosed calves has not yet been measured. This case report describes clinical findings and serum cTnI concentration in three doxycycline-overdosed calves.

Observation

A male, one-month-old Simmental calf weighing 44 kg (calf 1) was brought to Firat University Veterinary Animal Teaching Hospital because he had anorexia and lethargy. At presentation, the calf was apathetic, slightly dehydrated and dysphagic. Values for rectal temperature, pulse and respiratory rate were 39.3°C, 116 beats/minute, and 36 breaths/minute, respectively. The tongue of the calf was swollen and had no muscular tone. Leukocytosis (18.9 x 109/L, reference interval: 4.9–12 x 109/L ) and high plasma fibrinogen
concentration (8 g/L; reference interval: 2–7 g/L) indicated inflammation. An increased intensity of vesicular sounds was detected in the lung field. Thoracic ultrasonography revealed comet-tailing artifacts in the lung. History revealed that doxycycline hyclate (Hipradoxii, Hipra), total amount 1500 mg (which is 6.5 times the recommended dose of 5 mg/kg BW), had been administered orally to the calf 3 days previously to treat diarrhea. Based on the history and the results of clinical examination the calf was diagnosed with doxycycline overdose. Therapy included fluids, enrofloxacin (5 mg/kg BW i.m.; Baytril, Bayer), and meloxicam (0.5 mg/kg BW s.c., Bavet Meloxicam, Bavet); however, the calf progressively deteriorated and died on day 9. A post-mortem examination was not performed because the owner of the calf did not consent. Venous blood was collected from the jugular vein on admission (day 0), and on days 1, 3, 4, 8, and 9 for serum cTnI measurement (Table 1). Concentration of cTnI was determined with a human commercial cTnI assay (ADVIA Centaur TnI-Ultra, Siemens). The measurement range of the assay was 0.006–50.00 µg/L. The case history also revealed that two calves on the same farm were suffering from doxycycline overdose and another calf had died suddenly after doxycycline administration. The farm was visited to examine the calves. Two one-and-a-half-month-old Simmental calves (calf 2 and calf 3), weighing 70 kg, were examined. 1500 mg of doxycycline hyclate (which is about 4 times the recommended dose of 5 mg/kg BW) had been given orally to the calves. Physical clinical examination findings of calf 2 and calf 3 were normal. The calves were slightly anorexic but they were bright, alert, and responsive. No lesions were observed on the tongues of the calves and the tone of the calves’ tongues was strong. At the first farm visit, serum cTnI concentration of calf 2 and calf 3 was measured as 0.45 µg/L and 0.15 µg/L, respectively. The farm was visited to re-examine the calves two months later, the progress of the calves having been followed by phone calls to the owner during this interval. Calf 2 and calf 3 had a good appetite and were clinically normal. The serum cTnI concentration of calf 2 and calf 3 was measured as 0.01 µg/L at the second visit. Four clinically normal calves of a similar age as the doxycycline-overdosed calves from the same farm were used as the control, and had serum cTnI concentrations of 0.01, 0.03, and 0.08 µg/L.

**Discussion**

Sudden death, lethargy, lack of appetite, dysphagia, tongue paresis or paralysis, tachycardia, and respiratory distress have been observed in field occurring cases of doxycycline overdosing in calves [2,5,18]. It has been suggested that degenerative lesions determined in the *palatinus* muscle and tongue are likely to be responsible for the tongue paralysis, dysphagia, and pharyngeal paralysis [5]. Clinical findings of calves with experimental doxycycline overdosing were different from the clinical symptoms observed in field occurring cases of doxycycline overdosing. Only anorexia was observed, without tongue lesions and dysphagia, in calves with experimental doxycycline overdosing [3]. In the study reported here, calf 1 suffered from tongue dysfunction and dysphagia; however, decreased appetite was the only observation in calf 2 and calf 3. In this case report, the higher dose of doxycycline (6.5 times versus 4 times the recommended dose) resulted in the more severe clinical disorder, suggesting that the differences noted in the clinical findings may have resulted from the dose differences of doxycycline.

One of the major problems in doxycycline-overdosed calves are myopathies. Serum enzyme activities that show muscle damage were measured in doxycycline-overdosed calves and the results were inconsistent with each other. Brihoum et al. [3] determined absolutely no modifications in serum creatine kinase (CK), CK isoenzymes, lactate dehydrogenase, and aspartate aminotransferase (AST) activities in calves that experimentally received 5 times the recommended dose of doxycycline; however, increased CK and AST activities were determined in field occurring cases of doxycycline overdosing [2]. Necropsy and histopathology reveal severe tongue damage, with palatinus and striated muscle injuries in doxycycline overdosing cases [5]. Postmortem examination of 22 calves with doxycycline overdose revealed necrosis of the myocardium [2]. In a report, multifocal to diffuse, often well demarcated pale areas were observed in the heart of 11 of 16 veal calves with acute doxycycline intoxication. The endocardial or epicardial surfaces, as well as the full cut surface of the myocardium, had the lesions in the calves [5].

Although cardiac effects of doxycycline overdosing have been investigated in calves, no study measuring blood cTnI concentration in doxycycline-overdosed calves has not yet been published. Serum or plasma cTnI measurement is accepted as the gold standard biomarker to diagnose myocardial injury in human beings because of high sensitivity and myocardial tissue specificity [1]. Therefore measurement of serum or plasma cTnI concentration to detect myocardial damage has replaced previously used biomarkers. It is generally believed that human assays for cTnI can be used to measure blood concentration of cTnI in horses, sheep, goats, dogs, and cattle [17]. In the present study we measured

<table>
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<th>Time</th>
<th>Admission (Day 0)</th>
<th>Day 1</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 8</th>
<th>Day 9</th>
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<tr>
<td>cTnI</td>
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<tr>
<td>Concentration (µg/L)</td>
<td>29.4</td>
<td>10.6</td>
<td>1.60</td>
<td>0.82</td>
<td>0.092</td>
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**Table 1:** The results of serum cardiac troponin I measurement in calf 1.
serum cTnI concentration with ADVIA Centaur cTnI Assay. This assay was validated for cattle and it yielded sufficient analytical performance for the measurement of bovine cTnI [16]. Increased blood cTnI concentration due to myocardial damage was measured in horses, sheep, goats, and dogs [8,9,10,12]. Serum cTnI concentration was measured as 404 ng/mL in a horse with severe chronic focal myocardial coagulation necrosis [13]. The mean plasma concentration of cTnI for lambs with myocarditis was 146.78 ng/mL. [8]. High plasma cTnI concentration has been reported in a calf with myocarditis resulting from foot and mouth disease [7]. Elevated serum cTnI concentration was measured in a cow with tricuspid endocarditis [4]. In the current study increased serum cTnI concentrations in the calves with doxycycline overdose are similar to observations in rats that received a 10-fold overdose of doxycycline for 10 consecutive days [6]. The magnitude of increase in circulating cTnI was correlated with the severity of myocardial necrosis in cattle with monensin toxicosis and therefore it may be used to estimate the severity of myocardial damage in cattle [15]. We determined serum cTnI concentration of calf 1 as 29.4 µg/L at admission and the serum cTnI concentration on day 4 was lower than 1.04 µg/L. It was shown that marked myocardial cell necrosis was detected histopathologically in cows that had a cTnI concentration of > 1.04 ng/mL measured with ADVIA Centaur [15]. The serum cTnI concentration for the other two calves was higher than that of the calves used as the control but was < 1.04 µg/L.

In this report, calves with doxycycline overdose had increased serum concentrations of cTnI. Further studies are required to detect whether temporary myocardial damage occurs in doxycycline-overdosed calves.

References