

Original Research

Evaluation of Tenckhoff Catheter Use and Ceftriaxone Intraperitoneal Administration in Horses



Juliana de Moura Alonso^a, Thiago Yukio Nitta^a, Tatiana Yumi Mizucina Akutagawa^a, Amanda Paulino Crescencio^a, Regina Kiomi Takahira^b, Bruna dos Santos^b, Ana Liz Garcia Alves^a, Marcos Jun Watanabe^a, Celso Antônio Rodrigues^a, Rosângela Gonçalves Peccinini^c, Michel Leandro de Campos^c, Carlos Alberto Hussni^{a,*}

^a Department of Veterinary Surgery and Anesthesiology, School of Veterinary Medicine and Animal Science, University Estadual Paulista, Botucatu, São Paulo, Brazil

^b Department of Veterinary Clinic, School of Veterinary Medicine and Animal Science, University Estadual Paulista, Botucatu, São Paulo, Brazil

^c Department of Natural Active Principles and Toxicology, School of Pharmaceutical Sciences, University Estadual Paulista, Araraquara, São Paulo, Brazil

ARTICLE INFO

Article history:

Received 16 September 2016

Received in revised form 16 January 2017

Accepted 18 January 2017

Available online 28 January 2017

Keywords:

Antibiotics

Cephalosporins

Peritoneal catheter

Peritonitis

ABSTRACT

Peritonitis in horses persists with high incidence and mortality, requiring more innovative and effective therapeutic strategies. The aim of this study was to evaluate *Tenckhoff* catheters and intraperitoneal use of ceftriaxone in horses. Ten healthy, male horses, with an average age of 5 years, were used and divided into two groups of five animals each. A *Tenckhoff* catheter was implanted in both groups. The intraperitoneal group received 25 mg/kg of ceftriaxone diluted in 1 L of 0.9% saline solution (SS) intraperitoneally via the *Tenckhoff* catheter, and the intravenous group received 25 mg/kg of ceftriaxone intravenously and 1 L of SS intraperitoneally. In both groups, the dosing interval was every 24 hours for 5 days. The animals were evaluated clinically and with laboratory tests through a blood count and plasma fibrinogen assay. A macroscopic, physical-chemical, and cytological evaluation of the peritoneal fluid and an abdominal sonographic evaluation were conducted before the catheter implantation and at 1, 3, 5, 7, and 10 days after the implantation and ceftriaxone administration. Seven days after the catheter insertion and the beginning of the intraperitoneal treatment, a laparoscopic evaluation was performed. The *Tenckhoff* catheter proved to be an appropriate route for intraperitoneal solution administration; however, it promoted a moderate inflammatory response in the abdomen. No differences in inflammatory reaction was observed between groups, suggesting that the intraperitoneal administration of the drug did not trigger a local or systemic inflammatory process, amplifying the possibilities of intraperitoneal route utilization in the treatment of peritonitis.

© 2017 Elsevier Inc. All rights reserved.

1. Introduction

Peritonitis in horses has a varied etiology, being it possible to be primary or secondary. Most cases tend to be secondary, acute, diffuse, and septic [1]. Mortality rates

associated with this disease vary according to the underlying cause. Secondary peritonitis, related to intestinal rupture and postoperative colic presents mortality rates above 60% [2]. In contrast, primary peritonitis has survival rates that can reach 86% [3].

Established therapy for peritonitis in horses is based on supportive care and the combination of antimicrobials that provide coverage against gram-negative, gram-positive, and anaerobic bacteria. The most common association is penicillin, gentamicin, and metronidazole [2,4]. Despite the

* Corresponding author at: Carlos Alberto Hussni, Department of Veterinary Surgery and Anesthesiology, University Estadual Paulista, 18610970 Botucatu, São Paulo, Brazil.

E-mail address: cahussni@fmvz.unesp.br (C.A. Hussni).

use of this therapeutic strategy, secondary peritonitis persists with high mortality rates necessitating the investigation of procedures and drugs for peritonitis treatment to increase the survival rate of affected animals [5–8].

Abdominal drainage and lavage should have beneficial effects, such as removal of bacteria and cellular debris in the peritoneal cavity and decrease abdominal adhesions [7]. The intraperitoneal route promotes high antibiotic concentrations in the peritoneum and adjacent cells in the peritoneal cavity [8]; however, it is used without scientific confirmation of efficiency and has been poorly studied as only a single study in horses described the use of intraperitoneal antibiotics in the operative period [6].

Ceftriaxone is a third generation cephalosporin with established clinical efficacy, that is often used for primary peritonitis treatment [9] or associated with other agents for secondary peritonitis in humans [10]. Among the third generation cephalosporins, it has the highest antibacterial spectrum, acting against gram-positive, gram-negative, and anaerobic bacteria [11–15].

Tenckhoff catheters are traditionally used in humans for peritoneal dialysis and are considered a safe and reliable method of abdominal cavity access [16–18]. They are made of silicone and are straight or curve shape with additional holes to the lumen as well as two cuffs that, after deployment, are housed in the abdominal parietal muscles and subcutaneous tissue [17–19]. Despite the widespread use in humans, there are no reports of the *Tenckhoff* catheter use in horses.

The aim of this study was to evaluate the technical feasibility and safety of *Tenckhoff* catheter implantation and intraperitoneal administration of ceftriaxone in horses through clinical, laboratory, ultrasound, and laparoscopy evaluations.

2. Materials and Methods

2.1. Animals

Ten healthy male horses were used, six mixed breed and four Arabian horses, with an average age of 5.1 ± 1.3 years old and a mean body weight of 317.6 ± 26.9 kg. The animals

were housed in stalls, received coast cross hay and water *ad libitum*. Before the beginning of the study, the horses were subjected to a medical evaluation through clinical and laboratory tests.

The experiment was conducted in compliance with the Ethics Principles in Animal Experimentation, and it was approved by the Ethics Committee on Animal Experimentation (CEUA; Protocol #105/2013).

2.2. Constitution of Groups

The animals were randomly divided into two groups of five animals with a homogeneous distribution of breeds between the groups. Therefore, each group was composed of three mixed breed and two Arabian horses. The intraperitoneal group (IPG) received 25 mg/kg of ceftriaxone (Ceftriaxona sódica; Eurofarma, São Paulo, Brazil) diluted in 1 L of saline solution (SS) intraperitoneally via a *Tenckhoff* catheter every 24 hours for 5 days. The intravenous group (IVG) received 25 mg/kg of ceftriaxone intravenously every 24 hours for 5 days and 1 L of SS intraperitoneally for the same time and interval of administration. If the horses presented with clinical signs of local, abdominal, or signs of discomfort they would receive flunixin meglumine (1.1 mg/kg IV).

2.3. Peritoneal Catheter Implantation

The *Tenckhoff* dialysis catheter (Silmag Brasil; GMI, São Paulo, Brazil) is made of 100% silicone, 42 cm long, and has a 15 Fr diameter. It has a radiopaque line, a straight configuration, two Dacron cuffs, multiple additional holes to the lumen in its abdominal portion, and an extender 10 cm long with a Luer Lock connector (Fig. 1).

After 12 hours of fasting, the horses were restrained in stocks and sedated with detomidine hydrochloride (Dormium V-Agener União Ltda, Brazil) (bolus 5 µg/kg followed by continuous infusion of 20 µg/kg/h). The skin in the left flank region was clipped and aseptically prepared with chlorhexidine. The surgical site was infused with lidocaine 2% (Xylestesin-Cristália, produtos químicos e farmacêuticos Ltda, Brazil) for local anesthesia.

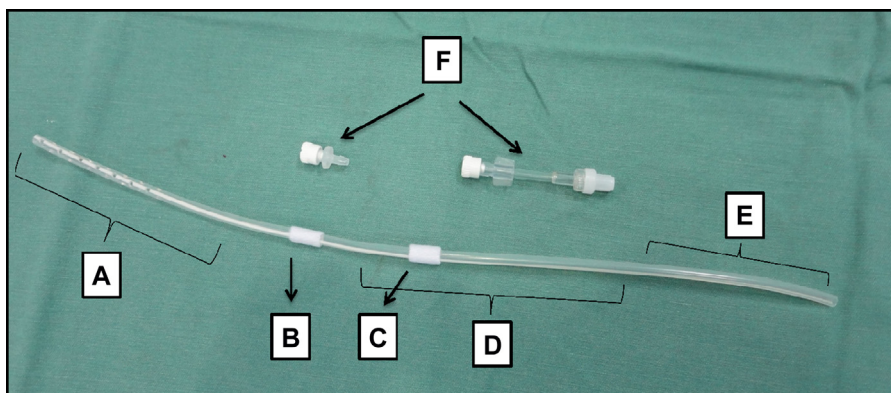


Fig. 1. *Tenckhoff* catheter. (A) Abdominal portion with multiple additional holes; (B) Muscular cuff; (C) Subcutaneous cuff; (D) Subcutaneous region; (E) External portion; (F) Extensor connectors.

An approximately 2 cm skin incision was made in the central region of the left paralumbar fossa at the height of the coxal tuberosity. The access was video-assisted by EndoTIP (Karl Storz Endoskope, Alemanha) cannula introduction with a rigid endoscope. The pneumoperitoneum was induced with CO₂ through the cannula, and the abdominal pressure during the procedure was maintained between 12 and 15 mm Hg.

After sufficient insufflation, the catheter was inserted through an additional portal, located 10 cm ventral and 5 cm caudal to the first access portal. One cuff was positioned in the abdominal muscles, and the other was positioned subcutaneously (Figs. 2A–F). Local anesthesia

of approximately 8 cm of the skin and subcutaneous tissue was provided for catheter passage in subcutaneous tunneling. For this procedure, a 5-mm trocar was used in the dorsal toward ventral direction (Figs. 2G–H).

The skin suture was performed with Nylon 0 (Mono-nylon-Brasuture, Ind Com Imp Exp, Indústria) in single separate standard. The catheter was connected to the extensor with a Luer Lock connector and attached to the skin with the same suture material (Fig. 2I). After skin fixation, a protective bandage with Micropore Tape (3M-Micropore TM, 3M Brazil) was applied. The dressing and protective bandage were changed daily.

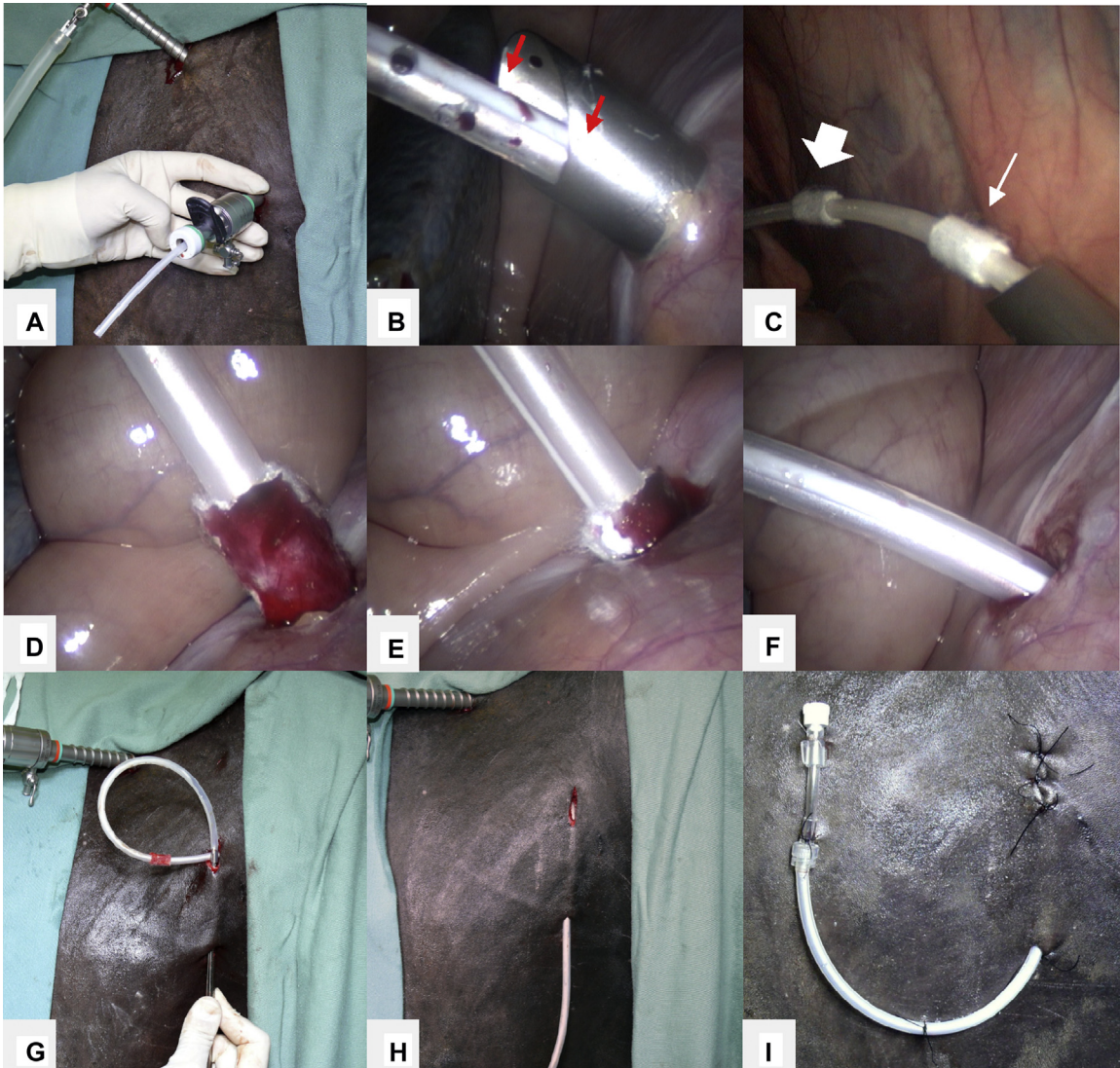


Fig. 2. Implantation and fixation of the *Tenckhoff* catheter. (A) Portal positioning and guided insertion of the catheter through the second portal; (B) Introduction of the catheter in the abdomen; the arrows indicate the additional lumen holes in the distal end of the catheter; (C) Introduction of the catheter; the arrows points to the Dacron cuffs. The large arrow points to the cuff that was housed in the abdominal muscle region, and the thin arrow points to the cuff to be housed in the subcutaneous region; (D) Retraction of the catheter for cuff positioning; (E) Passage and accommodation of the second cuff through the abdominal wall; (F) Final image of the abdominal wall after retraction and positioning of the cuffs; (G) Subcutaneous tunneling; (H) Catheter accommodated in the subcutaneous tunnel; (I) Skin after the suture and catheter attachment coupled to its extension tube.

2.4. Ceftriaxone Administration

After the end of the surgical procedure, the administration protocol was started for each group. Intraperitoneal administration followed the recommendations of antisepsis and environmental control as described by Bender et al [20].

The treatment was performed for 5 days to simulate real cases of septic peritonitis, in which treatment with antibiotics last at least 5 days.

2.5. Peritoneal Response to Tenckhoff Catheter Use and Intraperitoneal Administration of Ceftriaxone

The daily monitoring of the horses included evaluation of the heart and respiratory rates, color of the mucous membranes, capillary refill time, rectal temperature, and intestinal motility. The region of the subcutaneous tunnel and the catheter exit orifice were monitored for swelling, heat, and discharge.

Laboratory and ultrasound evaluations were performed before the Tenckhoff catheter placement (D0) and one (D1), three (D3), five (D5), seven (D7), and 10 days (D10) following the procedure.

Normal physiological parameters values were based on Feitosa [21] and hematological reference on Feldman et al [22].

Blood samples used to measure the complete blood count were collected through a vacuum system (Vacutainer-BD, Brazil) in the left cranial epigastric vein. The peritoneal fluid samples were collected in the linea alba region through a hypodermic needle 40 × 0.8 mm. A plain tube, without anticoagulant was used for chemical physical evaluation (pH, density, fibrinogen, glucose, protein) and an EDTA tube was used for cytology. Samples of blood and peritoneal fluid were processed immediately after collection.

The sonographic examination (MyLab70Vet, Esaote, Italy) evaluated the peritoneal reactivity by peritoneal fluid volume and echogenicity changes or the presence of fibrin and cellular debris. Echogenicity was graded in a system of scores, as follows: 0 (normal), 1 (slightly increased), 2 (moderately increased), and 3 (moderately increased, associated with the presence of cellular debris), and normality was established as the appearance of liquid before surgical procedure [23].

The location of the catheter in the abdominal parietal region and subcutaneous tunnel was evaluated for periluminal inflammatory reaction in the subcutaneous cuff region.

A laparoscopic inspection was performed 7 days after catheter implantation, with the preparation and procedure similar to the first laparoscopy. However, the access to the peritoneal cavity was located on the 18th intercostal space, approximately 8 cm below the transverse processes of the thoracic vertebrae. This procedure evaluated peritoneal reactivity related to drug aggression and the placement and patency of the catheter.

Peritoneal reactivity was divided into three score categories by a blinded surgeon: 0—no reactivity, 1—mild reactivity, and 2—moderate reactivity. This score degree was adapted from Alonso et al [23] adding the presence of local reaction due to catheter visceral contact.

The catheters were removed by traction on the 10th day and subjected to culture.

A long-term evaluation was performed 12 months after Tenckhoff implantation to evaluate the presence of abdominal adhesions or reactivity. This evaluation included sonographic evaluation, white blood cell (WBC) count, and peritoneal fluid analysis.

2.6. Statistical Analysis

As a result of a nonparametric distribution, the Mann Whitney test, with median values [24] were used to compare the groups at each time point, and the Wilcoxon test was used for paired samples [24] to compare the medians in each time point with the initial time point within each group. Significant differences were defined as $P < .05$.

3. Results

3.1. General and Specific Physical Examination

There were no significant differences between groups or time points for heart and respiratory rate, color of mucous membranes, capillary refill time, rectal temperature, or auscultation of intestinal motility. All parameters were within the physiological normal range. No horses required the administration of flunixin meglumine.

There were no signs of discomfort on intraperitoneal administration for either group. Two animals of the IPG showed serosanguineous secretion in the tunnel exit orifice between D5 and D10, which was not associated with the presence of local changes such as erythema, dolorous sensitivity on palpation, or local heat.

After catheter removal, fibrin clots were observed inside its lumen. No healing problems occurred with incisions and orifices after catheter removal.

3.2. Hematologic Evaluation

The IVG had a significantly higher WBC ($P < .0317$) on D1. Other parameters in the complete blood count were not significantly different. Within each group, the D0 leukocyte parameters were not significantly different from the other time points. Parameters for both groups were within the normal reference range ($< 14,500 \times 10^3/\mu\text{L}$) at all time points.

The IVG showed significantly higher plasma protein concentrations at D1, and these concentrations remained within the normal range in the animals of both groups (5.8–8.7 g/dL).

Plasmatic fibrinogen varied significantly ($P < .0477$) between D0 and D3 for IPG (Fig. 3). For both groups, there were time points when fibrinogen values exceeded the normal range (100–400 mg/dL); however, the median value did not exceed 400 mg/dL.

3.3. Peritoneal Fluid Macroscopic, Physicochemical, and Cytological Evaluation

Through chemical physical (pH, density, fibrinogen, glucose, protein) and cytology evaluation, although there was no significant difference in the peritoneal

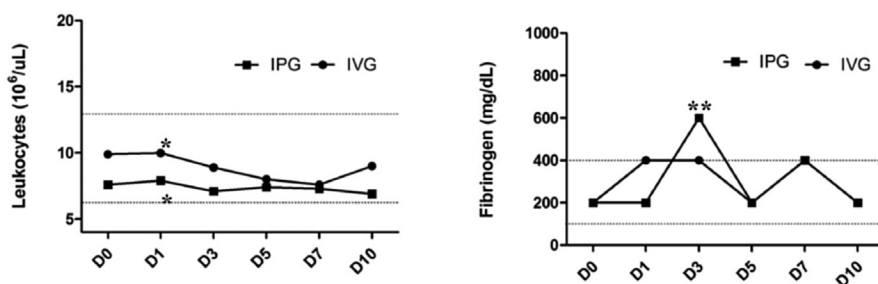


Fig. 3. Median values of leukocytes and plasmatic fibrinogen in IPG and IVG. * Significant difference between groups; ** Significant difference compared with the baseline. The dashed line represents the reference values for the species (leukocytes = 5.4–14.5 × 10⁶/μL; fibrinogen = 100–400 mg/dL). IPG, intraperitoneal group; IVG, intravenous group.

inflammatory response between groups, a clear increase in the inflammatory process was observed, especially on D5. This inflammation was noted through the turbid appearance of the liquid as well as by high nucleated cell counts and protein, not followed by the presence of bacteria in the peritoneal fluid and marked decrease in glucose levels (Fig. 4).

3.4. Sonographic Evaluation

Peritoneal fluid echogenicity increased after surgery at all time points. Between D5 and D10, the echogenicity increased was more pronounced, but no significant difference was observed between groups by scores comparison. An increased local inflammatory reaction with the presence of tissue disorganization and infiltrated fluid in subcutaneous cuff proximity was observed for both groups between D5 and D10 (Fig. 5).

3.5. Laparoscopic Evaluation

In the laparoscopic assessment carried out on D7, all animals showed turbid peritoneal fluid varying in color from dark yellow to orange. On the perimeter of the catheter at the point of entry through the abdominal wall, there was deposition of fibrin (Fig. 6).

The migration of the catheter in one animal was indicated by the presence of the muscle cuff inside the abdominal cavity (Fig. 6B). In all eight animals, the catheter presented with its curvature facing the dorsal region, often being housed under the nephrosplenic ligament (Fig. 6C), and in two animals, the catheter was positioned on the

intestinal segments (left large colon, small colon, or small intestine). After the catheters were visualized, 20 mL of SS were injected to examine their patency. All catheters were patent (Fig. 6D).

Laparoscopy showed that the presence of the catheter resulted in a localized inflammatory response in the region of contact with the viscera; however, no difference between groups was observed. The spleen was the most frequently affected structure, with strong fibrin deposition and thickening of the capsule (Fig. 6E), followed by the left dorsal colon serosa (Fig. 6F), which showed areas of suffusion. Among the animals that had localized inflammatory reactions, four presented exclusively in the spleen, and two presented in the spleen as well as in colon segments.

The inflammatory reaction scoring used to evaluate peritoneal reactivity showed no difference between groups. Animals that had mild or moderate peritoneal inflammation showed a higher congestion of vessels within the abdominal wall as well as in the intestinal segments.

3.6. Long-Term Evaluation

Ultrasound examination showed no abdominal adhesions between the abdominal wall and the spleen, spleen and intestinal segments, and/or between the intestinal segments (Fig. 7). The peritoneal fluid was normal and had an echogenic appearance similar to the preoperative period. The region of the subcutaneous tunnel was identified because of the presence of the scar on the skin evidencing the point of entry and exit of the catheter; no ultrasonographic changes were observed in the musculature and subcutaneous in the region of previous location of the tunnel.

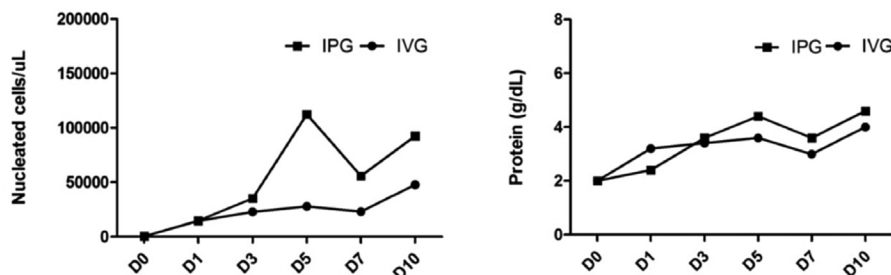


Fig. 4. Medians of nucleated cells and peritoneal protein concentrations in IVG and IPG peritoneal fluid. IPG, intraperitoneal group; IVG, intravenous group.

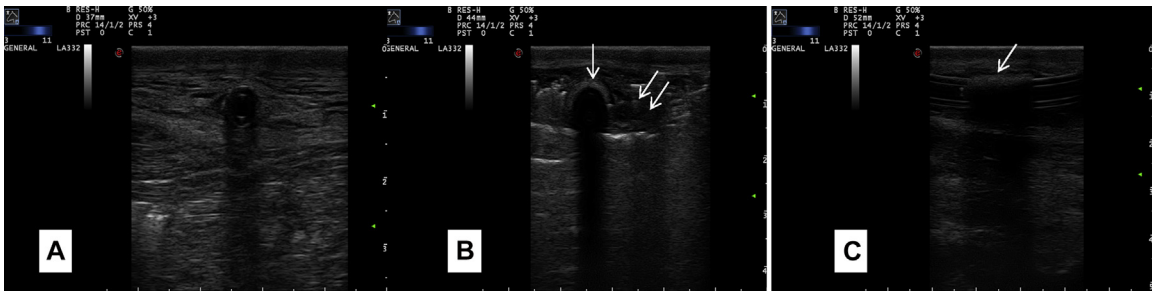


Fig. 5. Sonographic image of the subcutaneous tunnel region of an IPG animal in D10. (A) Transverse section of the *Tenckhoff* catheter; (B) Transverse section of the *Tenckhoff* catheter in the region of the subcutaneous cuff (arrow), demonstrating a periluminal inflammatory reaction (double arrow); (C) Longitudinal section of the catheter, demonstrating the presence of the subcutaneous cuff (arrow). IPG, intraperitoneal group.

The median values of WBC count for the IPG and IVG were, respectively, 9,200 and 10,150 after 12 months of surgery. The macroscopic, physical chemistry, and cytological evaluation

of the peritoneal fluid also showed all the features within the normal range, presenting, respectively, for IPG and IVG a median value of 670 and 530 nucleated cells (Fig. 8).

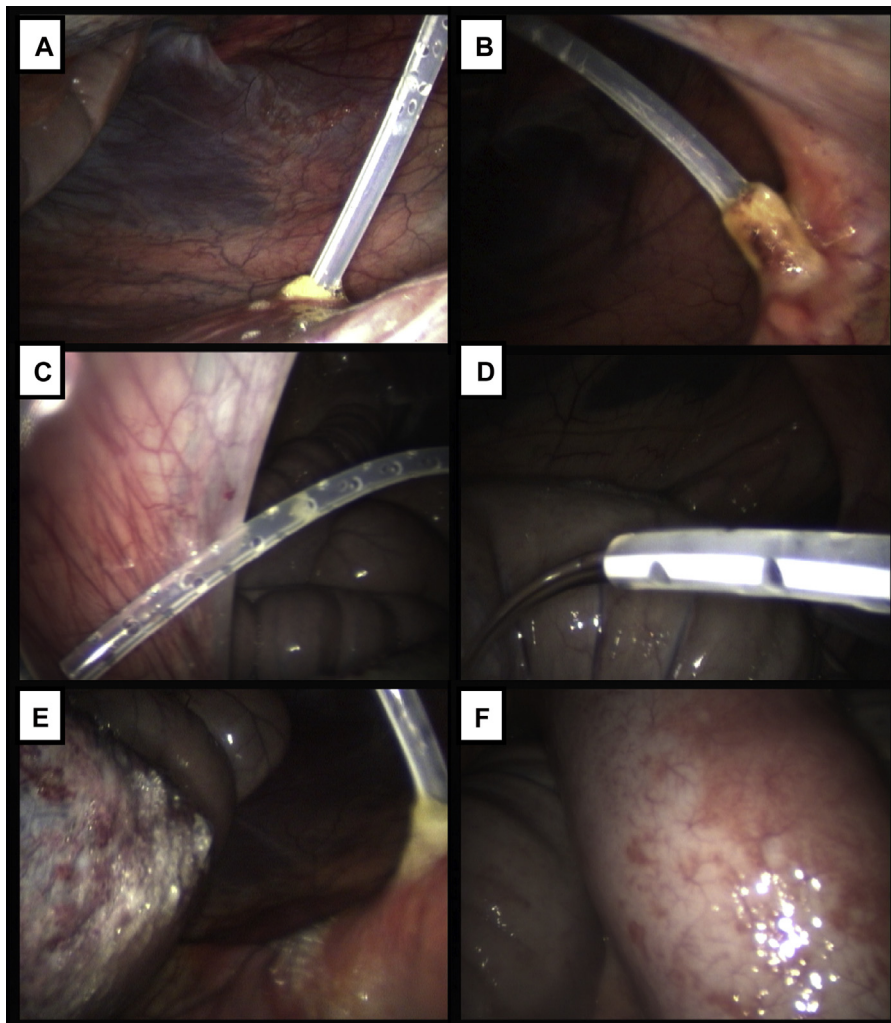


Fig. 6. Laparoscopic observations 7 days after catheter insertion. (A) Fibrin deposition around the entry point of the catheter into the abdominal cavity. (B) Muscle cuff migration into the abdominal cavity; (C) Catheter housed in the nephrosplenic ligament region; (D) Patency test of the catheter; (E) Presence of intense fibrin deposition on the contact point of the catheter with the caudal edge of the spleen, and the presence of inflammation and fibrin deposition around the catheter entry point; (F) Inflammatory reaction on the left dorsal colon resulting from contact with the catheter.

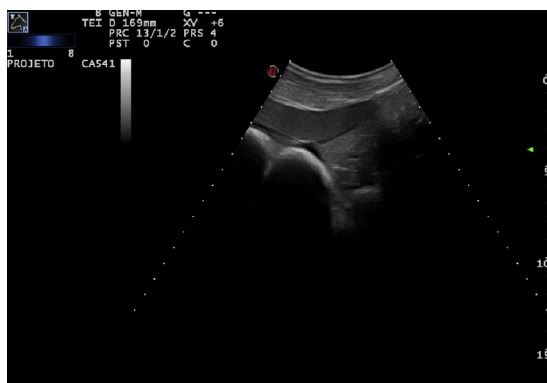


Fig. 7. Sonographic aspect of the caudal border of the spleen after 12 months of surgery. All animals showed free borders wrapped by a thin layer of peritoneal fluid.

4. Discussion

The *Tenckhoff* catheter was the object of study because of its widespread use with clinical safety in peritoneal dialysis in humans [17,25–27] and because of the fact that it is constituted of silicone, and described as a biocompatible material that allows the possibility of long-term use without stimulating local and systemic inflammatory responses [27,28]. Despite its apparent biocompatibility and the positive results in human studies, in the present study, we did find an inflammatory reaction on the viscera that came in contact with the catheter.

For the placement and maintenance of a peritoneal catheter in horses some particularities of the species, as an inhabitant of a contaminated environment should be considered, because of the risk of serious complications, such as septic peritonitis. Because of these considerations, *Tenckhoff* catheters have the advantage of the presence of Dacron cuffs that act as physical barriers to infection and stimulate a local inflammatory reaction with the consequent formation of fibrosis, which provides greater attachment of the catheter and reduces the risk of periluminal contamination [27].

The implantation of the *Tenckhoff* catheter may be accomplished percutaneously or laparoscopically [17,29,30]. Percutaneous deployment can be performed in any environment and has a lower cost, but it increases the

risk of bowel perforation [29,30]. The choice of video-assisted laparoscopic implantation allowed for good visualization of the peritoneal space and was reaffirmed as a safe and efficient method for positioning the catheter without complications [19].

There are no reports of using this type of catheter in horses, and the study was based on various aspects of its use in humans. In humans, the catheter is placed in the para-umbilical region. This location was considered inappropriate for horses because of the ventral location of the abdominal viscera that could obliterate the flow from the catheter. Thus, the region of choice was the medium dorsal of the left paralumbar fossa because this location reduces the risk of visceral iatrogenic puncture, prevents the compression of the catheter by the viscera, and enables a gravitational distribution of solutions. The subcutaneous tunneling was performed in the dorsal to ventral direction to allow drainage of possible secretions, preventing their accumulation and direction toward the abdominal cavity [16,27].

Infection at the catheter exit orifice is a major complication arising from the use of peritoneal catheters in humans [30–33]. Two animals in the IPG had serosanguinous secretions, which were associated with accumulation of fibrin in the tunnel exit opening, between the fifth and 10th days of maintenance. Because there were no signs of hyperthermia, local erythema, pain or heat, the local reaction was considered to be inflammatory in nature and not infectious [30–33]. These signs were not observed in either group. Dacron cuffs cause local reaction in the first days after catheter placement to provide greater attachment of the catheter and reduce the risk of periluminal contamination; however, the presence of an associated discharge with these local reaction is described as a complication [27]. In the two horses that had associated discharge, the local inflammatory reaction subsided after removing the catheter, suggesting that although silicon is considered a biocompatible material, the presence of the catheter and/or Dacron cuffs resulted in a periluminal inflammatory response. All catheters were sent to microbiology evaluation and no agents were found on culture.

Abdominal infection pathways in patients with peritoneal catheters include the following pathways: intraluminal contamination resulting from the administration of intraperitoneal solutions, allowing the entry of bacteria into the peritoneal cavity by the lumen of the catheter; periluminal contamination arising from the skin surface and entering

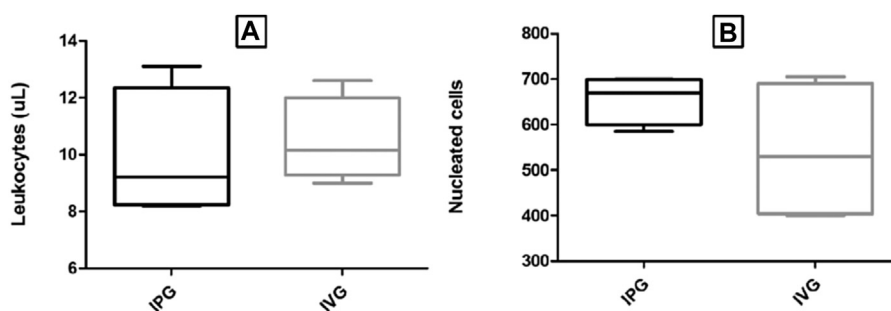


Fig. 8. Comparative values of IPG and IVG in a long-term hematological and peritoneal evaluation. (A) WBC count; (B) Peritoneal nucleated cell count. IPG, intraperitoneal group; IVG, intravenous group; WBC, white blood cell.

the peritoneal cavity from the peritoneal dialysis catheter tract; transmural contamination resulting from gut bacteria in the peritoneal cavity; and hematogenous contamination due to systemic infections [34]. Intraluminal and periluminal contamination are the most common pathways [34]. The model of antisepsis and protective bandages used in this study were adequate to prevent contamination of the abdomen. In spite of high nucleated cell counts in post-operative peritoneal fluid, no clinical signs of septic peritonitis were detected during catheter maintenance and no bacteria was found on cytology. Culture and peritoneal lactate should be of value if performed.

Fibrin deposition in the lumen of the catheter was evidenced by laparoscopic evaluation and at the moment of catheter removal. However, this accumulation did not result in any catheter patency change because there were no alterations in solution flow during the treatment period. No resistance was observed when laparoscopically injecting 20 mL of SS on the seventh day.

Clinical findings showed that neither intravenous nor intraperitoneal administration of ceftriaxone resulted in abnormalities of physiological variables. These results are different from the observations made by Ringger et al [13] and Gardner and Aucoin [35], who respectively used the dose of 50 mg/kg and 14 mg/kg and reported the occurrence of colitis, depression, and decreased appetite on administration of ceftriaxone. No adverse effects were observed by either route used in this study. Adverse effects from the use of ceftriaxone in humans are rarely reported, corroborating this study [36].

The choice of an antibiotic for intraperitoneal therapy was based on its pH and on the spectrum of action. A pH value below 5.5 or greater than 8.0 has been associated with complications for intravenous therapy, such as chemical phlebitis [37]. Ceftriaxone has a pH of 6.6, which is compatible with intravenous administration. Because ceftriaxone has been safely administered intravenously, it was initially considered to be suitable for intraperitoneal administration. Nevertheless, because of prolonged contact between the drug and the peritoneal cavity and organs, it was important to evaluate whether its presence may result in a local chemical reaction.

The differentiation of the inflammatory response origin was made difficult because of the possibility of being followed by ceftriaxone administration, laparoscopic procedure, and maintenance of the catheter. Both groups of animals developed signs of inflammatory peritoneal reaction. Because there were no significant differences between the hematological and peritoneal parameters between the groups, we concluded that the inflammation was caused by the laparoscopic surgery and catheter maintenance and not by the drug administration, suggesting that ceftriaxone may be used as an adjuvant treatment for septic peritonitis.

Laparoscopic surgery is classified as a minimum invasive procedure, that similar to open surgery affects the integrity and biology of the peritoneum [38]. The interference of an exploratory laparoscopic procedure was demonstrated in the seventh day, when was observed an increase in peritoneal fluid cells and protein. Postoperative evaluation of nucleated cell counts in a laparoscopic procedure for ovariectomy in six mares showed respectively

after 3 and 14 days of surgery median peritoneal cell counts of 23.050 cells/ μ L and 9.030 cells/ μ L [39]. These values are lower than ours and suggest that in spite of the laparoscopic procedure, the catheter may be the major stimulus to peritoneal inflammation.

The inflammatory response resulting from surgery and catheter insertion was restricted to the abdominal cavity and lasted as long as catheter maintenance, with no significant differences in WBC count profiles between groups. Although the IVG had higher WBC counts, both groups had parameters that remained within the normal range and showed no systemic inflammatory response associated with either the presence of the catheter or drug administration.

Intraperitoneal group plasma fibrinogen concentrations differed significantly between the baseline and after 3 days of drug administration. Fibrinogen elevation suggests that the acute inflammatory response was more intense in the IPG animals, but did not differ between groups. Plasma fibrinogen is an acute phase protein most commonly analyzed in plasma, and is a nonspecific indicator of an inflammatory reaction in horses [40]. It is noteworthy, however, that the plasma fibrinogen increase was not accompanied by a similar inflammatory leukocyte response in the blood analysis and peritoneal fluid of IPG.

The lack of a difference between the groups in echogenicity of peritoneal fluid in the sonographic examination confirms the clinical and laboratory findings that ceftriaxone was probably not the cause for the observed peritoneal inflammation. Despite the fact that *Tenckhoff* catheters are characterized as biocompatible, after the end of therapy with ceftriaxone, the echogenicity increases were maintained for both groups, and the laparoscopic examination showed a peritoneal inflammatory response resulting from visceral contact with the catheter in both groups.

5. Conclusions

The implantation, maintenance and use of *Tenckhoff* catheters in horses was feasible and safe for the evaluation period of 10 days; the *Tenckhoff* catheter resulted in mild to moderate abdominal inflammation because of contact with the viscera. A long-term evaluation showed no complications, such as abdominal adhesions. This study provided a precedent for this catheter use in horses for drug administration, dialysis, or abdominal lavage; however, the implantation in clinical cases should be evaluated because of the additional inflammation caused by the catheter implantation and because horses with septic peritonitis are prone for adhesions and fibrin accumulation what can interfere with the catheter patency.

Intraperitoneal administration of ceftriaxone did not result in greater local or systemic inflammatory responses. Studies are needed to assess the characteristic pharmacokinetics of ceftriaxone administered intraperitoneally and its use in clinical cases of peritonitis.

Acknowledgments

The authors declare no conflicts of interest.

Alonso JM and Hussni CA conceived and planned the study. Alonso JM, Hussni CA, Nitta TY, Crescencio AP, and

Akutagawa TYM participated in the execution of the study. Alonso JM, Hussni CA, Watanabe MJ, Alves ALG, Rodrigues CA, Peccinini RG, and de Campos ML contributed to writing and correction of the manuscript. Takahira RK and Santos B conducted laboratory tests.

This study received financial support from the São Paulo State Foundation for Research –FAPESP (grant number 2013/13799-7).

References

- [1] Browning A. Diagnosis and management of peritonitis in horses. *In Pract* 2005;27:70–5.
- [2] Hawkins JF, Bowman KF, Roberts MC, Cowen P. Peritonitis in horses: 67 cases (1985–1990). *J Am Vet Med Assoc* 1993;203:284–8.
- [3] Henderson ISF, Mair TS, Keen JA, Shaw DJ, McGorum BC. Study of the short- and long-term outcomes of 65 horses with peritonitis. *Vet Rec* 2008;163:293–7.
- [4] Davis JL. Treatment of peritonitis. *Vet Clin North Am Equine Pract* 2003;19:765–78.
- [5] Schein M, Hirshberg A, Hashnonai M. Current surgical management of severe intra-abdominal infection. *Surgery* 1992;112:489–96.
- [6] Faria EP, Marques JR, Alves GES. Características celulares e bioquímicas do líquido peritoneal de equinos submetidos à peritonite experimental. *Arq Bras Med Vet Zootec* 1999;51:335–44.
- [7] Nógrádi N, Tóth B, Macgillivray KC. Peritonitis in horses: 55 cases (2004–2007). *Acta Vet Hung* 2011;59:2.
- [8] Varghese JM, Roberts JA, Wallis SC, Boots RJ, Healy H, Fassett RG, Lipman J, Ranganathan D. Pharmacokinetics of intraperitoneal gentamicin in peritoneal dialysis patients with peritonitis (GIPD study). *Clin J Am Soc Nephrol* 2012;7:1249–56.
- [9] Alaniz C, Regal RE. Spontaneous bacterial peritonitis: a review of treatment options. *Pharmacol Ther* 2009;34:204–10.
- [10] Solomkin JS, Mazuski JE, Bradley AR, Rodvold KA, Goldstein EJC, Baron EJ, O'Neill PJ, Chow AW, Dellinger EP, Eachempati SR, Gorbach S, Hilfiker M, May AK, Nathens AB, Sawyer RG, Bartlett JG. Diagnosis and management of complicated intra-abdominal infection in adults and children: guidelines by the Surgical Infection Society and the Infectious Diseases Society of America. *Clin Infect Dis* 2010;50:133–64.
- [11] Bijie H, Kulpradist S, Manalaysay M, Soebandrio A. In vitro activity, pharmacokinetics, clinical efficacy, safety and pharmacoeconomics of ceftriaxone, compared with third and fourth generation cephalosporins: review. *J Chemother* 2005;17:3–24.
- [12] Ringger NC, Brown MP, Kohlepp SJ, Growall RR, Merrit K. Pharmacokinetics of ceftriaxone in neonatal foals. *Equine Vet J* 1998;30:163–5.
- [13] Ringger NC, Pearson EG, Gronwall R. Pharmacokinetics of ceftriaxone in healthy horses. *Equine Vet J* 1996;28:476–9.
- [14] Lamb HM, Ormrod D, Scott LJ, Figgitt DP. Ceftriaxone: an update of its use in the management of community-acquired and nosocomial infections. *Drugs* 2002;62:1041–89.
- [15] Albarellos GA, Kreil VE, Landoni MF. Pharmacokinetics of ceftriaxone after intravenous, intramuscular and subcutaneous administration to domestic cats. *J Vet Pharmacol Ther* 2007;30:345–52.
- [16] Tenckhoff J, Schechter H. A bacteriologically safe peritoneal access device. *Trans Am Soc Artif Intern Organs* 1968;XIV:181–7.
- [17] Nielsen PK, Hemmingsen C, Friis SU, Ladefoged J, Olgaard K. Comparison of straight and curled *Tenckhoff* peritoneal dialysis catheters implanted by percutaneous technique: a prospective randomized study. *Perit Dial Int* 1995;15:18–21.
- [18] Eklund BH, Honkanen EO, Kala AR, Kyllönen LE. Peritoneal dialysis access: prospective randomized comparison of the Swan neck and *Tenckhoff* catheters. *Perit Dial Int* 1995;15:353–6.
- [19] Ash SR. Bedside peritoneoscopic peritoneal catheter placement of *Tenckhoff* and newer peritoneal catheters. *Adv Perit Dial* 1998;14:75–9.
- [20] Bender FH, Bernardine J, Piraino B. Prevention of infectious complications in peritoneal dialysis: best demonstrated practices. *Kidney Int Suppl* 2006;70:44–54.
- [21] Feitosa FLF. *Semiologia Veterinária: A arte do diagnóstico*. 2 ed. São Paulo: Roca; 2008.
- [22] Feldman BF, Zinkl JG, JAIN CN. *Schalm's veterinary hematology*. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2000.
- [23] Alonso JM, Rodrigues KA, Yamada ALM, Watanabe MJ, Alves ALG, Rodrigues CA, Hussni CA. Peritoneal reactivity evaluation in horses subjected to experimental small colon enterotomy and treated with subcutaneous heparin. *Vet Med Int* 2014;2014:385392.
- [24] Pagano M, Gauvreau K. *Principles of biostatistics*. California: Duxbury/Thomson Learning; 2000. p. 285–301.
- [25] Gokal R, Ash SR, Helfrich GB. Peritoneal catheters and exit-site practices: toward optimum peritoneal access. *Perit Dial Int* 1993;13:29–39.
- [26] Ash S. Chronic peritoneal dialysis catheters: effects of catheter design, materials and location. *Semin Dial* 1990;3:39–46.
- [27] Hagen SM, Lafranca JA, Ijzermans JN, Dor FJ. A systematic review and meta-analysis of the influence of peritoneal dialysis catheter type on complication rate and catheter survival. *Kidney Int* 2014;85:920–32.
- [28] El-shahat YI, Cruz C. The impact of catheter design on preventing CAPD complications. *Saudi J Kidney Dis Transpl* 1995;6:275–9.
- [29] Tsimoyiannis ECT, Siakas P, Glantzounis G, Toli C, Sferopoulos G, Pappas M, Manataki A. Laparoscopic placement of the *Tenckhoff* catheter for peritoneal dialysis. *Surg Laparo Endo Per* 2000;10:218–21.
- [30] Poole GH, Tervit P. Laparoscopic *Tenckhoff* catheter insertion: a prospective study of new technique. *Aust N Z J Surg* 2000;70:371–3.
- [31] Lobo JVD, Villar KR, Andrade MP, Bastos KA. Preditores de peritonite em pacientes em um programa de diálise peritoneal. *J Bras Nephrol* 2010;32:156–64.
- [32] Li PK, Szeto CC, Piraino B, Bernardini J, Figueiredo AE, Gupta A. Peritoneal dialysis-related infections recommendations: 2010 update. *Perit Dial Int* 2011;31:512.
- [33] Abud ACF, Santos LKMA, Rodrigues FFL, Damasceno MMC, Zanetti ML. Peritonite e infecção de orifício de saída do cateter em pacientes em diálise peritoneal no domicílio. *Rev Lat Am Enfermagem* 2015;23:902–92.
- [34] Leehey DJ, Gandhi VC, Daugirdas JT. Peritonite e infecção do local de saída. In: Daugirdas JT, Blake PG, Ing TS, editors. *Manual de diálise*. 3a ed. Rio de Janeiro: Guanabara Koogan; 2003.
- [35] Gardner SY, Aucoin DP. Pharmacokinetics of ceftriaxone in mares. *J Vet Pharmacol Ther* 1994;17:155–6.
- [36] Brogden RN, Ward A. Ceftriaxone: a reappraisal of its antibacterial activity and pharmacokinetic properties, and an update on its therapeutic use with particular reference to once daily administration. *Drugs* 1988;35:604–15.
- [37] Crepaldi RMC, Monteiro C, Peterlini MAS, Pedreira MLG. Potencial hidrogeniônico de antimicrobianos, segundo os fatores ambientais temperatura e luminosidade. *Rev Lat Am Enfermagem* 2010;18:278–86.
- [38] Brokelman WJA, Lensvelt M, Borel Rinkes IHM, Klinkenbijn JHG, Reijnen MMPJ. Peritoneal changes due to laparoscopic surgery. *Surg Endosc* 2011;25:1–9.
- [39] Pader K, Freeman LJ, Constable PD, Wu CC, Snyder PW, Lescun TB. Comparison of transvaginal natural orifice transluminal endoscopic surgery (NOTES) and laparoscopy for elective bilateral ovariectomy in standing mares. *Vet Surg* 2011;40:98–1008.
- [40] Campbell MD, Bellamy JE, Searcy GP. Determination of plasma fibrinogen concentration in the horse. *Am J Vet Res* 1981;42:100–4.