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Neural Therapy in a multidrug-resistant urinary tract infection in a cat: case report

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Abstract Urinary tract infection is a frequent condition in companion animals, where several pathogens may be involved, among them, multidrug-resistant agents to antimicrobials, making their treatment difficult. In this context, adjuvant therapies can be indicated to assist in the treatment. Thus, the objective of this study was to report the antimicrobial action of a solution containing procaine hydrochloride associated with sodium bicarbonate, intravesically administered, in a male feline (domestic cat) with urinary tract infection due to multidrug-resistant microorganism. The cat with a history of urinary infection developed after urethrostomy was attended. The animal was receiving treatment with the antimicrobial amoxicillin with clavulanate however, without positive clinical and laboratory response. After performing urine culture and antibiogram, where the microorganism *Proteus mirabilis* resistant to 18 classes of tested antimicrobials was isolated, an intravesical application of 2.0 mL of 0.7% procaine solution plus sodium bicarbonate was performed. After seven days of this application, a new urine culture and antibiogram were performed, which did not show any growth of microorganisms. It is concluded that the 0.7% procaine hydrochloride solution associated with intravesical sodium bicarbonate showed antimicrobial action against multi-resistant *Proteus mirabilis,* which causes urinary infection in a cat.

Keywords: neural therapy, cystitis, microorganisms, infection, local anesthetic

1. Introduction

In the pet clinic, the frequency of animals with urinary tract infections (UTI) is high. There are several pathogens associated with this infection, with the presence of multidrug-resistant agents to antimicrobials being more and more frequent (Fongaro 2011). According to Bahr Arias et al (2008), Gram-negative microorganisms are the most frequently found in infections by multidrug-resistant agents. Antimicrobial therapy is the treatment of choice for these infections and should be chosen based on the result of the antibiogram (Ferreira et al). In the current medical clinic, most animals with urinary tract infections need to start treatment before obtaining the results of culture and antibiogram tests (Ferreira et al 2014).

Thus, therapies such as neural therapy can be indicated in order to assist or even start the treatment of these patients. Neural Therapy has its theoretical bases in Russian physiology of the mid-19th century, having been advocated by Pavlov, Speransky, Vischevsky, and Bikov in Russia, by Spiess, Leriche, and Schleich in Germany, and by Head in England (Cruz and Fayad 2011). Procaine and lidocaine in low concentrations (0.1 to 1%) were and still are the drugs used in this therapy for the treatment of people and animals (Cruz and Fayad 2011). Thus, this therapy consists of administering these drugs in different body regions of the patient for therapeutic and non-anesthetic purposes, according to the patient's life history (Castro 2011; Gonçalves et al 2020).

Since 1906, Spiess has observed the anti-inflammatory action of procaine. In 1925, Ferdinand and Walter Huneke successfully treated a migraine unresponsive to their sister's treatments and other clinical conditions through the application of intravenous procaine and reported a possible electrical action and the distance of this drug (Vianna and Gonçalves 2020). According to Cruz and Fayad (2011), the stimulus triggered by local anesthetics stimulates the restoration of the physiological potential (sodium and potassium pump) of affected cells since these diluted drugs have a repolarizing action due to their dielectric characteristic. According to Vianna and Gonçalves (2020), 0.7% procaine hydrochloride has up to 207 mV. The normal cell has an electrical resting potential that varies from + -40 to + -90 millivolts, resulting from the presence of sodium and potassium ions. If there are constant, strong, or irritating stimuli, the cell may lose its ability to repolarize, remaining depolarized. 0.7% procaine works as a dielectric substance that electrically activates cells, allowing cell repolarization, and the exchange of ions by the plasma membrane, allowing physiological cell restoration.

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According to Gonçalves et al (2020), Neural Therapy can be successful in conditions such as interstitial cystitis (Pandora's Syndrome), in addition to being able to assist in the treatment of joint, bone, dermatological, neurovegetative diseases, herpetic neuralgia, chronic pharyngitis, renal lithiasis, distemper, megaesophagus, atopic dermatitis, that is, it can be indicated for several inflammatories, infectious and behavioral pathologies. This therapy can be associated with other treatments, and it can even be used in pregnant, lactating, and young animals.

Procaine or lidocaine, following the principles of neural therapy, can be used in various forms, such as ointments, nebulizers, eye drops, nasal drops, in a perilesional, intravenous, peri organic way, in the spinal canal, in the surgical, intra-arterial wound, zones Head, metamers, trigger points, intravenous, acupuncture, and intraperitoneal points (Gonçalves et al 2020). In this context, this therapy can be used in order to help or even treat urinary tract infection before obtaining the results of the urine culture and the antibiogram; or as adjuvant drugs in the treatment against multidrug-resistant bacteria (Gonçalves 2020). Also, Gonçalves (2020) found that the association of procaine hydrochloride and sodium bicarbonate had antimicrobial action *in vitro* against *Staphylococcus aureus and Proteus mirabilis* that cause urinary infection.

Thus, the objective of this study was to report the antimicrobial action of 0.7% procaine hydrochloride solution associated with sodium bicarbonate, administered intravesically in a cat with urinary tract infection due to multidrug-resistant microorganism.

2. Casuistry

A two-year-old mixed-breed cat was seen with a history of pelvic limb paresis due to a vertebral fracture after being run over. The animal was being treated with acupuncture and physiotherapy. However, after 30 days of surgery, it was necessary to perform a penectomy with a urethrostomy. After 40 days of urethrostomy, the animal presented with cystitis, with the presence of dysuria and hematuria, being treated with the antimicrobial amoxicillin with clavulanate (EMS S/A - Germed Farmacêutica LTDA – Jaguariúna,SP, Brazil) (22 mg/kg) every 12 hours, for 21 days, associated with acupuncture sessions. Through this treatment, there was clinical and laboratory improvement in the animal. After 120 days of this condition, the animal again presented clinical manifestations of hematuria, dysuria, and lack of appetite, which was diagnosed with urinary tract infection. Thus, on that occasion, urine was collected by cystocentesis guided by ultrasound (Figure 1), for urine culture with antibiogram, and treatment with amoxicillin + clavulanate (EMS S/A – Germed Farmacêutica LTDA - Jaguariúna, SP, Brazil) (22 mg/kg) was started every 12 hours, until the results of the exams. Through this therapy, there was a return in appetite and water intake, but the animal continued to present hematuria and dysuria, and mild prostration. After seven days of urine collection and the start of antimicrobial therapy, the culture and antibiogram results were obtained. The microorganism isolated in the urine was *Proteus mirabilis*, resistant to 18 classes of tested antimicrobials, including the antibiotic that had been prescribed for the start of treatment. The antimicrobials tested were as follows: amikacin 30 mcg, amoxicillin with clavulanic acid 30 mcg, azithromycin 15 mcg, cefadroxil 30 mcg, cephalexin 30mcg, cephalothin 30 mcg, ceftiofur sodium 30 mcg, ceftriaxone 30 mcg, clindamycin 0,2 mcg, doxycycline 30 mcg, enrofloxacin 06 mcg, erythromycin 15 mcg, streptomycin 10 mcg, gentamicin 10 mcg, minocycline 30 mcg, nitrofurantoin 300 mcg, norfloxacin 10 mcg, and sulfamethoxazole with trimethoprim 23,75/1,25 mcg. The test was by disk diffusion and the interpretation by CLSI (Clinical Laboratory Standard Institute).

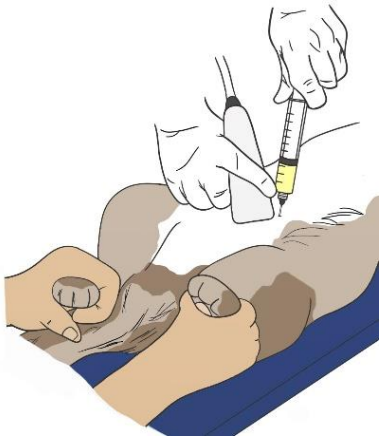

Figure 1 Cystocentesis guided by ultrasound.

As the animal had presented a clinical improvement with the instituted therapy, it was decided to keep the prescription of amoxicillin with clavulanate for seven days and to institute an adjuvant therapy with the intravesical application by cystocentesis of 2.0 mL of the procaine hydrochloride solution a 0.7% associated with sodium bicarbonate (Figure 2). The solution was prepared using 250 mL of 0.9% sodium chloride solution (JP Indústria Farmacêutica. Ribeirão Preto, SP, Brazil)

plus 3.5 mL of 50% procaine hydrochloride (Casa das Formulas, Belo Horizonte, MG, Brazil) and 5.0 mL of 8.4% sodium bicarbonate (Samtec, Ribeirão Preto, SP, Brazil). Twenty-four hours after this application, the animal's urine no longer had blood, and after 48 hours, the animal no longer had dysuria, with significant clinical improvement. Seven days after the intravesical application of the procaine solution, a new urine collection was performed by cystocentesis for urine culture and antibiogram, where no microorganism growth was observed.

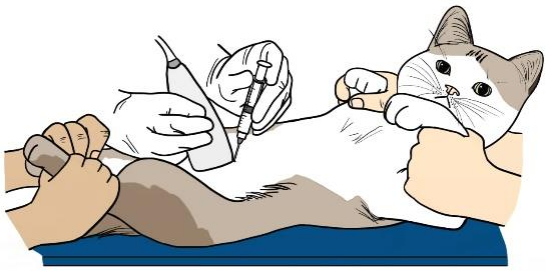

Figure 2 Intravesical application of 2.0 mL of the procaine hydrochloride solution a 0.7% associated with sodium bicarbonate.

3. Discussion

Recurrent urinary tract infection (UTI) is one of the most common complications reported after urethrostomy in cats. This fact was observed in the animal in this report, where, 40 days after the urethrostomy surgical procedure, the first episode of urinary tract infection presented. At this moment, the treatment chosen was using the antimicrobial amoxicillin with clavulanate, which according to Carvalho et al (2014), is one of the drugs of choice as the first option for the treatment of UTI. The choice of the antibiotic was successful since there was an improvement in the animal's clinical and laboratory conditions. However, four months after this treatment, the animal developed a urinary tract infection again. As it was the second episode of the infection, with a relatively short time, it was decided to perform a urine culture and antibiogram. Given the clinical condition of the patient, who was prostrate with intense hematuria and dysuria, it was decided to start antibiotic therapy before the results of the exams, as recommended by Olin and Bartges (2015). These authors suggested that antimicrobials should be used to treat UTI, even before the result of urine culture and susceptibility testing. Since the result of the use of amoxicillin with clavulanate in the previous episode of infection was satisfactory, where there was remission of the infection, the same antimicrobial was prescribed to start the treatment.

The isolated agent in urine culture was *Proteus mirabilis*, a Gram-negative bacterium, which according to Bahr Arias et al (2008), is one of the Gram-negative microorganisms commonly related to multidrug-resistant infections. Fact observed in this case, since the microorganism *Proteus mirabilis* was resistant to 18 classes of antimicrobials, including beta-lactams, aminoglycosides, and quinolones. According to Shrestha et al (2019), antimicrobial resistance is characterized when the agent is resistant to three or more classes of antimicrobials. In view of the result of the multidrug resistance of the isolated urine agent, it was decided to institute a complementary therapy with the use of the local anesthetic procaine associated with sodium bicarbonate in order to assist the treatment of urinary tract infection because, according to Labedan (1988), in Gram-negative bacteria, such as *Proteus mirabilis*, local anesthetics can induce changes in the fluidity of the cytoplasmic membrane and induce bacterial growth inhibition. Also, according to Dokai et al (2018), the action of sodium bicarbonate can be enhanced in association with another antimicrobial, such as a local anesthetic.

The 0.7% procaine solution plus sodium bicarbonate was used in this case because, as demonstrated by Gonçalves (2020) in his study, this solution promoted the *in vitro* growth inhibition for 48 hours of *Proteus mirabilis*. Fact that was observed in this report with its use since after the application of the intravesical solution in the animal, clinical improvement was observed, and in the urine culture, there was no longer the presence of the microorganism, thus verifying the antimicrobial effect of the solution.

According to Reuter et al (2017), procaine also has an anti-inflammatory, anti-rheumatic, anticancer action and increases cellular vitality. In a comparative study with dexamethasone, procaine was shown to have better anti-rheumatic and joint protective action after intra-articular applications in rats with osteoarthritis. Furthermore, procaine hydrochloride, in addition to its anti-inflammatory and antimicrobial functions, works as a dielectric substance that electrically activates cells, allowing cell repolarization, the exchange of ions through the plasma membrane and allowing the physiological reestablishment of cells, thus allowing to reestablish cellular balance body.

4. Conclusions

Thus, it is concluded that the 0.7% procaine hydrochloride solution associated with intravesical sodium bicarbonate showed antimicrobial action against multi-resistant *Proteus mirabilis,* which causes urinary infection in a cat. Thus, this is a treatment option in multi-resistant and unresponsive infections to other antimicrobials.

Conflict of Interest

The authors have no conflict of interest to declare.

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