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Universidade Estadual Paulista “Júlio de Mesquita Filho”
Faculdade de Medicina Veterinária e Zootecnia

EFEITO ANTIMICROBIANO *in vitro* DE TERAPIAS BIOLÓGICAS E NÃO BIOLÓGICAS EM MICRORGANISMOS CAUSADORES DE ENDOMETRITE EM ÉGUAS

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Fevereiro – 2023

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Dissertação apresentada junto ao programa de Biotecnologia Animal para obtenção do título de MESTRE.

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RESUMO

A endometrite é a principal causa de subfertilidade em éguas, podendo ser de origem infecciosa ou não infecciosa. O diagnóstico de endometrite se dá pela associação de diferentes técnicas a fim de identificar a presença de neutrófilos e de microrganismos nos casos infecciosos. O tratamento se dá por uma abordagem multimodal, sendo comumente associadas lavagens uterinas, agentes ecbólicos, anti-inflamatórios e antimicrobianos. Contudo, com o aumento de resistência antimicrobiana, o desenvolvimento de terapias alternativas às tradicionais se faz necessário, uma vez que, a utilização de antimicrobianos na rotina à campo promove o desenvolvimento de microrganismos multirresistentes. Assim, o presente trabalho, no capítulo 1 apresenta uma revisão bibliográfica ressaltando a endometrite, classificações, formas de diagnóstico e principais tratamentos, apresentando tratamentos alternativos às terapias tradicionais que possam evitar o desenvolvimento de microrganismos multirresistentes. Já, o capítulo 2 apresenta o artigo no qual foi testada a atividade antimicrobiana de terapias alternativas contra microrganismos causadores de endometrite em éguas. Este estudo teve como objetivo avaliar o efeito antimicrobiano *in vitro* de terapias alternativas (NTT) utilizadas na prática clínica contra microrganismos causadores de endometrite em éguas. O experimento foi dividido em terapias não-biológicas, sendo estas: Dimetilsulfóxido (DMSO), Peróxido de hidrogênio (H_2O_2), ringer ozonizado (O_3, 60µg/ml de ozônio durante 10 minutos), Iodopovidona 4% (Iodine), e terapias biológicas: plasma rico em plaquetas (PRP, 1056±198 $x10^3$plaquetas/µl) e plasma pobre em plaquetas (PPP, 37±14 $x10^3$plaquetas/µl). Os microrganismos testados foram *Escherichia coli (E.coli), Pseudomonas aeruginosa (Pseudo), Klebsiella pneumoniae (Kleb), Staphylococcus aureus (Staph),* e *Candida albicans (Candida).* Dentre as terapias alternativas não-biológicas, a H_2O_2 apresentou os melhores efeitos inibitórios *in vitro*. Já, das terapias alternativas biológicas, o PRP foi mais eficiente quando comparado ao PPP. Assim, a H_2O_2 e o PRP apresentaram-se eficientes na inibição de microrganismos causadores de endometrite em éguas, contudo, estudos *in vivo* são necessários para avaliar o efeito clínico das terapias.

Palavras-chave: endometrite infecciosa, equinos, resistência antimicrobiana, subfertilidade

ABSTRACT

Endometritis is considered the leading cause of subfertility in mares, being infectious or non-infectious. The diagnosis of endometritis is done using different techniques to identify the presence of neutrophils and microorganisms on infectious cases. Treatment is based on a multimodal approach that commonly associates uterine lavage, ecbolic agents, anti-inflammatories and antibiotics. However, within high levels of antimicrobial resistance, new non-traditional therapies are necessary, once, indiscriminate use of antimicrobials in the field promotes multidrug-resistant microorganisms' development. Thus, at the Chapter 1, it was performed a literature review, emphasizing the endometritis, classifications, diagnosis, treatments and alternative therapies that have been used to avoid antimicrobial resistance development. Besides that, on Chapter 2, there is an article where it was assessed the antimicrobial activity of alternative therapies against microorganisms that causes endometritis in mares. This study aimed to assess the *in vitro* antimicrobial effect of alternative therapies (NTT) that are commonly used to treat infectious endometritis. The experiment was subdivided in non-biological therapies as: Dimethylsulfoxide (DMSO), Hydrogen Peroxide (H_2O_2), ozonated ringer (O_3, 60µg/ml of ozone for 10 minutes), Povidone-iodine 4% (Iodine); and biological therpaies: platelet-rich (PRP, 1056±198 $x10^3$platelets/µl) and platelet-poor plasma (PPP, 37±14 $x10^3$platelets/µl). The microorganisms that were tested were: *Escherichia coli (E.coli), Pseudomonas aeruginosa (Pseudo), Klebsiella pneumoniae (Kleb), Staphylococcus aureus (Staph),* and *Candida albicans (Candida).* Of non-biological alternative therapies, H_2O_2 presented the best *in vitro* inhibitory effects, and of biological alternative therapies, PRP was more effective when compared with PPP. Thus, H_2O_2 and PRP presented good *in vitro* effects to inhibit microorganisms causing endometritis in mares, however, *in vivo* studies are necessary to evaluate the clinical effect of each therapy.

Key-words: antimicrobial resistance, equine, infectious endometritis, subfertility

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