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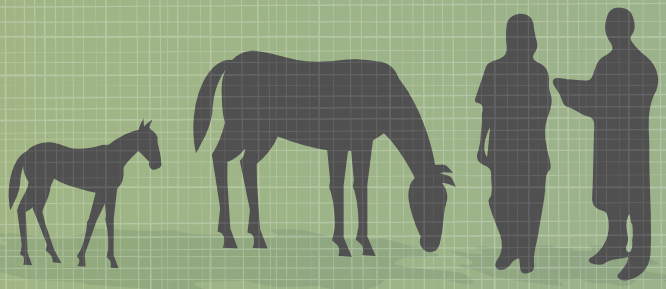

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CAT: Should we use systemic or intra-uterine antibiotics to treat bacterial endometritis

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Clinical scenario

In practice, clinicians are regularly presented with mares with acute or chronic endometritis requiring treatment. Practitioners first need to identify the causative agent(s) involved and, in an era where practitioners have a greater appreciation of, and responsibility for, antibiotic stewardship, the antibiotic sensitivity pattern of the agent(s) involved needs to be determined to facilitate appropriate antibiotic therapy. There are many facets to the treatment of bacterial endometritis in the mare; however, antibiotic therapy is generally considered the mainstay of therapy, with uterine lavage, with or without other nonantibiotic additives, considered secondary or adjunctive therapies. Antibiotics can be used systemically or locally via the intra-uterine route. Many clinicians use intra-uterine therapy with perceived success; however, many of the licensed equine antibiotics are being used 'off label' via the intra-uterine route. Regardless of this, local therapy is a desirable option as it may be possible to reduce the total effective dose of antibiotics used to treat the infection.

PICO question

In mares affected by bacterial endometritis, is systemic antibiotic therapy more effective than intra-uterine therapy?

Search strategy

Abstracts on the Pubmed/Medline (https://pubmed.ncbi.nlm.nih.gov/) database were searched from 1967 to 2022 using the following criteria: All fields were searched for ((equine) or (horse) or (mare)) and ((uterine) or (endometritis)) and (((antibiotic) or (antibacterial)) or ((treatment) or (therapy))) and ((minimum inhibitory concentration) or (MIC) or (pharmacokinetics) or (tissue concentration) or (serum concentration)) or ((systemic) or (intra-uterine) or (uterine)). In addition searching of references within the author's knowledge was conducted.

Quantity of evidence

The initial Pubmed search retrieved 240 abstracts; relevance screening was conducted on these abstracts identifying 27 papers relevant to the question. A further 9 papers were located from the author's knowledge, giving a total of 35 papers. The publication date range was from 1978 to 2020.

Quality of evidence

Of the 36 papers, 18 were experimental pharmacokinetic studies investigating systemic antibiotic delivery including endometrial tissue concentrations; 10 were experimental pharmacokinetic studies investigating intra-uterine antibiotic delivery; 3 were experimental pharmacokinetic studies investigating and comparing intra-uterine and systemic antibiotic delivery; 4 were experimental studies looking at the effects of intra-uterine infusion of antibiotics on the endometrium; and 1 was an experimental study looking at the efficacy of antibiotic therapies in traditional culture medium and equine post-partum uterine fluid.

In reviewing the evidence, it was clear that there was not going to be enough appropriate evidence to answer this question. There are no controlled studies investigating the efficacy of systemic or intra-uterine antibiotics in treating endometritis, either individually or in comparison. There is, however, some evidence to suggest that intra-uterine administration of antibiotics may be advantageous over systemic therapy. A study by Orsini and co-workers [1] demonstrated that endometrial tissue concentrations of amikacin were higher when it was infused into the uterus vs. systemically at a much lower dose of 4.4 mg/kg (2.0 g intra-uterine dose) compared with 14.5 mg/kg by i.m. injection. As amikacin is a concentration-dependent antibiotic, higher peak concentrations at the site of infection will optimise bacterial killing.

On the other hand, it is acknowledged that application of intra-uterine antibiotics has a weakness; the antibiotics must stay in the locality, within the uterus, to be efficacious and not voided through an open cervix. Additionally their absorption may be influenced by concurrent application of other therapies [2]. Other factors such as infusion volume can have an influence over absorption and/or endometrial tissue concentrations [3]. The evidence also demonstrates that there are some antibiotics that one should avoid using via the intra-uterine route. Rodriguez and co-workers [4] demonstrated that certain commercial preparations of enrofloxacin, namely Baytril (Elanco UK AH Limited), are severely irritating to the uterus. Severe inflammatory changes were also noted following the intra-uterine infusion of oxytetracycline [5].

In recent years there have been some additions to the literature looking at antibiotics used systemically, demonstrating that appropriate minimum inhibitory concentrations (MIC) are achieved in endometrial tissues and therefore would likely appropriately treat susceptible bacterial agents (**Table 1**).

Table 1: Published systemic antibiotic dosages and routes of administration of antibiotics accessible in the UK in the treatment of endometritis caused by susceptible organisms

Antibiotic	Route	Dose	Reference
Amikacin	i.v. or i.m.	10 mg/kg once a day	[1]
Ceftiofur hydrochloride	i.m.	2.2 mg/kg once a day	[6]
Doxycyxline hyclate	orally	10 mg/kg twice a day	[7]
Enrofloxacin	i.v.	5 mg/kg once a day	[8]
Gentamicin	i.v.	6.6 mg/kg once a day	[9]
Sulfadiazine and trimethoprim	orally	24 mg/kg twice a day	[10]

Summary

Much more research is required to understand the advantages and disadvantages of intra-uterine vs. systemic therapy in an in vivo model. There will likely be many factors which influence intra-uterine antibiotic absorption and local retention. For the concentration-dependent antibiotics such as the aminioglycosides, the intra-uterine route may be advantageous from the point of view of enhanced endometrial concentrations and bacterial killing; however, this has to be balanced against potential toxicity and irritation the antibiotic may cause to the endometrium.

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