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INTRA-VENOUS ADMINISTRATION OF COBACTAN 4.5%® AND INTRAUTERINE CEFQUINOME CONCENTRATIONS IN THE MARE

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Endometritis is the most important cause of reduced fertility in the mare. In the cow cefquinome has successfully been used in parenteral administration for the treatment of endometritis and in previous studies cefquinome has been proven to be safe both for the endometrium and equine sperm cells (Amirids et al., 2003; Parlevliet et al., 2006; Parlevliet et al., 2007). No data are available about the cefquinome concentrations in the uterus of the mare after intravenous administration. The purpose of this study was to measure the concentration of cefquinome (Cobactan 4.5%® IV, Intervet International, Boxmeer, the Netherlands) in the endometrium of the mare, after a single intravenous treatment to determine whether this drug would reach a significant concentration in the endometrium and if there persistence of cefquinome. No data are available about the intravenous use of cefquinome and its concentration in the uterus of the mare.

Ten clinically healthy cycling barren mares of known cytology and bacteriology with no abnormalities on palpation and ultrasound of the reproductive system and less than 5 mm intrauterine fluid at admission were selected for the trial. All mares were allocated at random to the treatment and before treatment with cefquinome cytology and bacteriology of the uterus were performed.

The mares were treated intravenously with cefquinome (Cobactan 4.5%® IV; 1 mg/kg (600 mg in 11 ml solvent) (T=0)) when a follicle > 30 mm, uterine edema and cervical relaxation were present. Endometrial biopsy's (0.5 g) were taken at 2, 6 and 24 hrs after treatment with cefquinome, frozen in liquid nitrogen (-196°C) and stored until further analysis. Palpation of uterus, cervix and ovaries and ultrasound of uterus throughout once daily oestrus were evaluated according to a routine protocol for breeding. Cefquinome concentrations (ng/g) (mean ± SD) in the endometrial tissue samples were quantified using a high-performance liquid chromatography (HPLC) assay. For statistical analysis of cefquinome concentrations at different time points a Student T-test was used.

All mares did ovulate within 1.8 ± 0.79 days after treatment and 0.8 ± 0.79 days after the last biopsy. Five out of ten mares showed a positive cytology (signs of inflammation) at the start of the experiment. Initially eight mares were positive on bacteriology. The concentrations of cefquinome found in the endometrial tissue in the first hours after administration were higher than the MIC90 known for the most common bacterial species in the mare’s uterus (Table 1). Variation in endometrium cefquinome concentrations between mares was found. The mean concentrations remained above the MICs for at least 6 hours for E.coli (MIC90 = 0.125µg/ml), S.zooepidemicus (MIC90=0.03 µg/ml) and K. pneumoniae (MIC90=0.06 µg/ml). However for P. aeruginosa the concentrations did not reach the MICs (4 - 8 µg/ml) after single treatment (Thomas et al., 2003).

After sampling mares (n=8) were artificially inseminated with 300 million TNM (total number of progressive motile spermatozoa with normal morphology) and even mares with positive cytology or bacteriology became pregnant (n=4). All 4 non-pregnant mares showed a positive bacteriology result and one also a positive cytology.

The cefquinome concentrations in the uterus remain above the MIC90 values of the most common bacterial species in the horse for more than 6 hours after a single intravenous injection. The concentrations (ng/g) of cefquinome found in the endometrial tissue in the first hours after a single intravenous treatment were higher than the MIC90 known for the most common bacterial species in the mare’s uterus (Thomas et al., 2006; Thomas and Thomas,
When compared with the cefquinome concentrations reached in plasma after IV administration of 1 mg/kg to adult horses (Allan and Thomas, 2003), quite similar mean values are observed: 1231 ng/ml (2h), 211 ng/ml (6h) and 0 (24h). This shows the good diffusion of cefquinome into the endometrial tissue. However in previous experiments it was shown that intra-uterine infusion of cefquinome provides higher concentrations (Parlevliet et al., 2007). The data may even suggest that cefquinome is more slowly eliminated from the endometrial tissue than from the plasma. Therefore Cobactan 4.5% will be a valuable antibiotic for intravenous use to treat the equine (post-breeding) endometritis at the dosage of 1 mg/kg once or twice daily depending on the pathogen involved. The one-day IV treatment could be used to treat post-breeding endometritis which regularly occurs in the horse after breeding if *Streptococcus spp* are suspected while 12 hrs intervals should be used to treat Gram negative bacteria.

**References**


**Table 1:** Cefquinome concentrations\(^1\) (ng/g) (mean ± SD) in endometrial biopsies taken from 10 mares at each time point after one single intravenous treatment with Cobactan 4.5% IV.

<table>
<thead>
<tr>
<th>Hours after treatment</th>
<th>1-day cefquinome (ng/g) (mean±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>984.76±843.31</td>
</tr>
<tr>
<td>6</td>
<td>270.60±250.38</td>
</tr>
<tr>
<td>24</td>
<td>16.17±35.75</td>
</tr>
</tbody>
</table>

\(^1\) The values < LOQ (25 ng/g) or when cefquinome was not detected were considered to be 0 in the calculation of the means (and SD) (P<0.05).