The Influence of pH on Antimicrobial Substances in Canine Vaginal and Urethral Secretions

Udo Hoyme, Axel Baumueller, and P. O. Madsen

Urology Section, Veterans Administration Hospital and Department of Surgery, School of Medicine, University of Wisconsin, Madison, Wisconsin, USA

Accepted: September 5, 1977

Summary. Trimethoprim and rosamicin (a new basic macrolide antibiotic) were administered to normal and oophorectomised female dogs by constant intravenous infusion before and after oestrogen and androgen administration. Their concentrations in plasma and in urethral and vaginal secretions were determined by bioassay and correlated with the pH values of vaginal and urethral secretions. Both compounds were concentrated in the vaginal and urethral secretions in reverse correlation with the pH of these fluids. Trimethoprim and rosamicin have antimicrobial spectra well suited for the treatment of bacterial urethritis and vaginitis and require further clinical investigation.

Key words: Trimethoprim - Rosamicin - Vaginal and urethral secretions.

The mode of drug secretion by the urethral epithelium as well as by the female paraurethral glands, referred to as Skene's glands (6) or the female prostate (9), a terminology supported by embryological studies (3), seems to have many analogies with prostatic secretion in the male (2). Lipid solubility and a basic pKa are the necessary requirements for the secretion of antibacterial agents into the acid urethral and prostatic secretions in concentrations exceeding the simultaneous plasma concentrations (4). Protein binding appears to be of less importance.

The mechanism of diffusion and concentration of drugs in the acid vaginal secretion is similar and also occurs by nonionic diffusion across the vaginal epithelium. The difference between theoretical and true concentration gradients (vaginal secretion/plasma) may be explained by the lack of permanent trapping of vaginal secretion in the compartment since continuous seepage of vaginal secretion occurs (7). The influence of partial cervical excretion cannot be excluded (5).

In view of the nonionic diffusion of antibiotics with basic pKa into acid secretions, we were interested in investigating the influence of pH-changes of urethral and vaginal secretions on the antibacterial concentration ratios between these secretions and plasma. It was expected that with decreasing pH, the ratios would increase, resulting in higher antimicrobial substance concentrations in the vaginal and urethral mucosa.

In this study, we have investigated the distribution of trimethoprim (pKa 7.3) and rosamicin (pKa 8.7) (a new macrolide antibiotic with activity against gram-positive as well as gram-negative bacteria, chlamydia and mycoplasms) in plasma and urethral or vaginal secretions in dogs in relation to varying pH-values, induced either by oophorectomy of hormone application, or both.

1 Trimethoprim, RO 5-6846, was supplied by Hoffman-LaRoche Inc., Nutley, NJ.
2 Rosamicin was supplied as Rosamicin sodium dihydrogen phosphate by Schering Corp., Bloomfield, NJ.
MATERIALS AND METHODS

Six adult female dogs weighing 17.6 ± 4.4 kg (mean ± 1 SD) were anaesthetised with sodium thiopental intravenously and a bilateral oophorectomy was performed. After a period of at least 42 days, studies were carried out as described below and the results compared to a control group of six other adult female dogs not being in oestrus and weighing 15.8 ± 2.6 kg. Three dogs from each group received either trimethoprim or rosamicin.

For the collection of specimens of urethral and vaginal secretions the dogs were anaesthetised with sodium thiopental intravenously, and the urethra was occluded at the bladder neck by a tourniquet to prevent urine entering the urethra. The bladder was drained by a suprapubic Foley catheter. The vaginal wall was then exposed with a speculum and cytological specimens were obtained, fixed, and stained according to the Papanicolaou technique for the purpose of evaluating the hormonal status of the vaginal mucosa. When sufficient fluid was available, the pH of urethral and vaginal mucosa was measured by a BMS 3 Mk 2 Blood Micro...