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BII-32

PLACENTAL TRANSFER OF LOCAL ANESTHETICS (LA): PREDICTIONS FROM A PHYSICOCHEMICAL MODEL.

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Local anesthetics (LA) are commonly used drugs during labor. Despite their epidural or subarchnoidal application, maternal plasma levels are clinically relevant. In addition, LA produce many early (CNS depression, hypotension, jaundice) and long lasting (low rating in neurocognitive scores) neonatal side effects indicating certain placental transfer. Thus, a kinetic model of placental transfer could be useful to predict LA neonate's plasma levels.
LA are cationic drugs, so their permeability and degree of compartmental trapping are pH dependent. Our model, running in MS Excel 2003 worksheet for Windows®, Microsoft Corp, allows calculate the LA compartmental trapping (Rb) and theoretical neonate concentrations for a given pH.
If neonatal pH lies between 7 – 7.2 in an optimum labor conditions, the obtained Rb (1.4 – 2.3 according to each pH and LA) would indicate that neonate concentrations doubled the maternal concentrations. These data correlate well with the observed dose dependent side effects of LA.

BII-33

PHARMACOLOGICAL STRATEGIES TO IMPROVE IVERMECTIN EFFICACY AGAINST RESISTANT NEMATODES.

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The involvement of the efflux-transport protein P-glycoprotein (Gp-P) on both the pharmacokinetic disposition and resistance mechanisms to macrocyclic lactones has been described. This work aimed to study the effects of loperamide (LPM), a Gp-P modulating agent, on ivermectin (IVM) pharmacokinetics and efficacy against resistant nematodes in sheep. Eighteen Corriedale lambs naturally infested with gastrointestinal nematodes were assigned into three experimental groups. Group A remained as untreated control. Other animals (Groups B and C) received ivermectin either alone or co-administered with LPM (0.2 mg/kg, 2 times every 12 h). Blood samples were collected between up to 14 days post-treatment and IVM plasma concentrations were determined by HPLC. The pattern of efficacy was estimated by the faecal egg count reduction test (FECRT) and adult nematode counts. LPM enhanced the IVM plasma availability (47 %) in co-administered lambs. The FECRT values were increased from 79 % to 96 % in the presence of LPM. The general efficacy against nematodes was increased from 48 % to 77 % after the LPM co-administration. The clinical relevance of this pharmacokinetic/pharmacodynamic interaction is under study in our laboratory.

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PHARMACOKINETICS OF CEFOPERAZONE IN NORMAL AND MASTITIC GOATS.

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Cefoperazone is a 3th generation semisynthetic cephalosporin antibiotic active against Gram-positive and Gram negative bacterias. In the present experience, six healthy lacting goats were used (Trial 1), these same animals were later induced with mastitis (Trial 2). In both Trials the animals recibed two doses of cefoperazone (Lab. Richet) by intramammary route (100 mg). Milk non-compartmental pharmacokinetic values in normal and mastitic glands were determined. Results. Elimination half-life ($t_{½}$) (Trial 1) 9.3 ± 1.9, (Trial 2) 11.9 ± 3.5 h; the area under the curve [$AUC_{(0\text{-}108)}$] (Trial 1) 7040.2 ± 3491.1, (Trial 2) 21044.0 ± 22319.9 $\mu g.ml^{-1}.h$ and the mean residence times (MRT) (Trial 1) 9.5 ± 1.9 and (Trial 2) 10.3 ± 4.7 h.
The results suggest that cefoperazone milk concentrations were high until 48 hours after second dose administration. Residues were detected in normal and mastitic milk during 108 hours postadministration of the antibiotic.

BII-35

PHARMACOKINETIC OF CEPHALEXIN AFTER INTRAVENOUS AND INTRAMUSCULAR ADMINISTRATION TO DOMESTIC CATS.

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Introduction: Cephalexin (CFX) is a first generation cephalosporin widely used in domestic animals for the treatment of grampositive (Staphylococcus spp., Streptococcus spp.) and gramnegative (Escherichia coli, Proteus spp) infections. The aim of this study was to analyze the serum disposition of CFX after intravenous (IV) and intramuscular (IM) administration to cats and, to correlate plasma concentrations with the minimum inhibitory concentrations (MIC) for pathogen bacteria isolated from cats.
Materials and Methods: 5 and 6 adult cats received 10 mg/kg of CFX by IV and IM administration, respectively. Blood samples were withdrawn at pre-determined times over an 8 h period. CFX serum concentrations were determined by microbiological assay using Micrococcus luteus (ATCC 9341) as test micro-organism. Plasma disposition curves were analyzed by non linear methods. CFX MIC were determined for 11 Staphylococcus spp., 5 Streptococcus spp. and 8 E. coli by macrodilution broth method.
Results: Main pharmacokinetic parameters were: C_{pmax}: 44.15±14.64 μg/ml (IV) and 19.84±5.59 μg/ml (IM); $AUC_{(0\text{-}\infty)}$: 57.64±18.64 μg.h/mL (IV) and 40.37±6.12 μg.h/mL (IM); $V_{d(ss)}$: 0.41±0.14 L/kg; $t_{½}$: 1.66±0.24 h (IV) and 1.73±0.31 h (IM); MRT: 2.16±0.35 h (IV) and 2.28±0.36 h; Cl_B: 0.19±0.06 L/h.kg. Plasma CFX concentrations were above MIC=1 μg/ml for 6 and 8 h after IV and IM administrations, respectively.