Enrofloxacin crosses equine placenta in early pregnancy without inducing gross lesions in fetus

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Ongoing studies in our laboratory suggest that administration of enrofloxacin to late term pregnant mares does not induce lesions in the fetus or resulting foals. However, organogenesis occurs early in pregnancy and it is possible that fluoroquinolone exposure will affect initial cartilage and bone formation during this period. We hypothesized that enrofloxacin administration to early pregnant mares results in high concentrations of both enrofloxacin and its active metabolite ciprofloxacin in fetal fluids and that fluoroquinolone exposure in early pregnancy induces chondrotoxic lesions in the 60 day fetus. Objectives were to: (i) determine enrofloxacin and ciprofloxacin concentrations in fetal fluids when enrofloxacin is administered at therapeutic doses during early pregnancy; and (ii) compare endochondral ossification of long bones from those fetuses with gestationally age matched controls. Mares carrying normal pregnancies (45 days) were assigned to 2 groups, control (n = 7) or a therapeutic dose of enrofloxacin (7.5 mg/kg PO, n = 6). Enrofloxacin was administered orally every 24 hours for 14 days Abortion was induced on day 15 by administration of 500 µg cloprostenol. Fetal heart rate was monitored via transrectal ultrasonography every 6 hours and the fetus removed manually when no heartbeat was detected. After removal, samples of allantoic and amniotic fluids were aspirated with an 18 gauge needle and preserved at - 80ºC until analysis. Limbs, heart, lung, liver, kidney, and placenta were fixed in 10% formalin for histological analysis. All tissues were stained with H&E. Fetal limbs were sectioned in the sagittal plane to include the whole limb and were also stained with Toluidine blue and Masson's trichrome to assess cartilage and extracellular matrix. Slides were evaluated by a board-certified pathologist blinded to treatment group. Enrofloxacin and ciprofloxacin concentrations in fetal fluids were measured by L MS/MS (5500 QTRAP LC/MS/MS system Sciex, Framingham, MA). Software Analyst 1.6.2 was used for data acquisition and analysis. Mares aborted at 62 ± 0.5 days of gestation, and mean time from last enrofloxacin treatment to abortion was 41 ± 7.5 hours, with no difference between treated and control mares. Enrofloxacin and ciprofloxacin were detected in both amniotic (223.2 ± 160.6 and 58.5 ± 36.3 ng/ml, mean ± SEM) and allantoic fluids (326 ± 118 and 102.5 ± 19.6 ng/ml) of treated mares. No differences were noted in histological features of the front or hind limbs of fetuses in the control and enrofloxacin exposed experimental groups. Fetal stage of development and ossification of the bones of the limbs was comparable between groups. Short term administration of enrofloxacin in early pregnancy did not result in apparent pathologic lesions in the equine fetus. Although further research is needed to assess other stages of pregnancy, longer durations of treatment and long term foal outcomes, enrofloxacin may be useful to treat select severe bacterial infections in pregnant mares.

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