VERAPAMIL INFLUENCES THE PHARMACOKINETICS AND TRANSPLACENTAL EXCHANGE OF MOXIDECTIN IN PREGNANT SHEEP

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In pregnant sheep at 120 - 128 days of gestational age, a study was done to evaluate the effect of the co-administration of verapamil (Vpm) and moxidectin (MXD) on the maternal and fetal disposition kinetics after intravenous administration of MXD. Ten pregnant Suffolk Down sheep of 63.6 ± 9.2 kg body weight (bw) were surgically prepared to insert polyvinyl catheters in the fetal femoral artery and vein and amniotic sac. The ewes were randomly assigned to two experimental groups. In group 1 (control), 5 ewes were treated with an intravenous bolus of 0.2 mg MXD/kg bw. Group 2 (Vpm-MXD), 5 ewes were subcutaneously treated with Vpm (2.5 mg/kg x 3 doses at 12 h intervals) and 0.2 mg/kg MXD by intravenous route. Maternal and fetal blood samples were taken before and after MXD administration during a 144 h post-treatment period. Samples were analyzed by liquid chromatography (HPLC). A non-compartmental pharmacokinetic analysis was performed and statistical differences were determined using the Mann-Whitney U test. Differences were considered significant at \( P < 0.05 \).

Significantly lower levels in MXD maternal plasma concentrations were found after co-administration of Vpm/MXD in comparison with the group treated with MXD alone. In the Vpm/MXD treated group the volume of distribution and clearance values were higher than that observed in the control group \( (P < 0.05) \). A significant increase in MXD fetal area under the plasma concentrations’ curve was observed in the group of fetuses from pregnant ewes treated with Vpm/MXD.

The results of our study have demonstrated that pharmacological blockage of P-glycoprotein with Vpm can increase the maternal volume of distribution and the transplacental transfer of MXD to fetal circulation.

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