STUDIES ON THE PREGNANT MARE AND NEWBORN FOAL

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The two studies reported herein are part of ongoing research to determine the source, normal and abnormal concentrations and biological significance of a group of steroids related to progesterone. Many of these compounds are chemically reduced and thus may be simple metabolic end-products. However, since some are known to have biological activity in other species, and concentrations in pregnant mares and dysmature foals are extremely high, these compounds may have important regulatory function in the equine.

In the first study, plasma progestins in newborn foals were quantified by gas chromatography - mass spectrometry. In normal foals (n=3) 5-pregnene-3β,20β-diol (P5-$\beta\beta$) increased from birth to 6 hr and thereafter declined to 72 hr (3.1 ± 1.0, 6.4 ± 1.1 and .09 ± .01 μg/ml, respectively (mean ± sem); 5α-pregnane-3β,20β-diol (5α-$\beta\beta$) similarly increased and decreased (1.2 ± .7, 1.3 ± .8 and .3 ± .2μg/ml at 0, 6 and 24 hr, respectively). Pregnenolone, 5-pregnene-3β,20α-diol, 5α-pregnane-3β,20α-diol and 3β-hydroxy-5α-pregnan-20-one were highest at birth (2.3 ± .4, .5 ± .1, .8 ± .4 and .5 ± .1 μg/ml, respectively) and declined gradually and were low or nondetectable at 72 hr; progesterone, 5α-pregnane-3,20-dione and 20α-hydroxy-5α-pregnan-3-one were not detected. Treatment of normal foals with ACTH (.22 IU/kg bwt, i.v., n=3) did not affect pregnane concentrations; as previously reported cortisol is increased by this treatment. In three dysmature foals P5-$\beta\beta$ and 5α-$\beta\beta$ were generally lower at birth than in normal foals and increased gradually to maximum at 48 hr for P5-$\beta\beta$ (16.2 ± 7.3 μg/ml) and 24 hr for 5α-$\beta\beta$ (.8 ± .1 μg/ml). All other pregnanes generally declined from birth in dysmature foals but were considerably higher than in normal foals at 48-72 hr. These data suggest metabolism of pregnenolone to other pregnanes is abnormal in dysmature foals, characterized primarily by accumulation of the 20β-hydroxylated products P5-$\beta\beta$ and 5α-$\beta\beta$.

In the second study, two reduced progestins were tested in pony mares for their biological effects on inhibiting equine LH (eLH) and ovulation. Pony mares were treated daily (50 mg, im) with 5α-pregnane-3,20-dione (5α-DHP, n=9) or 3β-hydroxy-5α-pregnan-20-one (3β-5α-DHP, n=4) from Day 6 through Day 18 postovulation plus a luteolytic dose of $PGF_2\alpha$ (5 mg, im) on Day 8; control mares (C, n=6) received only $PGF_2\alpha$ on Day 8. Days from treatment to ovulation were not different between C, 5α-DHP and 3β-5α-DHP groups (13.3 ± .4, 14.9 ± 1.2 and 14.3 ± .2 days, respectively, mean ± s.e.m.) However, two mares in the 5α-DHP group had delayed ovulations (19 and 21 days) which was similar to progesterone-$PGF_2\alpha$ treated mares (positive controls) in which ovulation was delayed to 21.5 days. Concentrations of eLH on Day 13 (mean day of ovulation in C mares) were lower ($P<.05$) in 5α-DHP treated mares (44.3 ± 6.1 ng/ml) but not different in 3β-5α-DHP treated mares (68.8 ± 2.6 ng/ml) when compared to C mares (64.1 ± 7.6 ng/ml) on their day of ovulation. These data

indicate the reduced progestin 5α-DHP does inhibit eLH and delays ovulation in some mares but this level of treatment is not sufficient for complete inhibition as observed following similar progesterone treatment.

Further studies are underway to determine the biological effects of these compounds in vivo during early pregnancy and in vitro by studying their metabolic pathways.