Serum oxytocinase activity in control, pregnant, oxytocin, and carbetocin treated mares at the expected time of luteolysis

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Oxytocin in horses is involved in uterine clearance, luteal maintenance, parturition, passage of fetal membranes, maternal-foal bonding, and milk let-down. Oxytocinase/insulin regulated aminopeptidase (IRAP) or leucyl-cystinyl aminopeptidase (LNPEP) is an enzyme that is involved in the regulation of hormones such as oxytocin and vasopressin, and little is known how oxytocin is metabolized. The objective of this study was to characterize oxytocinase (OTase) activity in serum in control, pregnant, oxytocin, and carbetocin treated mares at the expected time of luteolysis. Light horse mares were examined daily in estrus until the day (D) of ovulation (D0), and then on D12, D13, D14, D15 with transrectal palpation and ultrasonography. Jugular blood samples were obtained from D12 to D15 after ovulation. Mares were randomly assigned to treatment, with a rest cycle in between treatment cycles. Groups were: control (n=8), pregnant (Preg) (n=6), (bred using artificial insemination with >200 million normal and motile sperm from one fertile stallion every other day in estrus), oxytocin (Oxy) (n=6) (Oxytocin, Bimeda, MTC, Cambridge, ON, Canada) 60 IU BID IM D7 to 14) and carb (n=4) (T.R.C., North York, ON, Canada; 1.19 mg SID IM D7 to 14). Serum was separated and stored frozen until analysis. A commercial ELISA (LNPEP for horses, MyBioSource, San Diego, CA) with a detection range of 6.25–200 U/L and an intra and interassay coefficient of variation of <15%, which was validated in our laboratory, was used for the analysis. Proprietary software (STATA/SE version 13.1, College Station, TX) using p<0.05 was used to evaluate the normality of the OTase data using a Shapiro–Wilk test, and Kruskal Wallis was used to evaluate the effect of treatment and day on OTase. Post hoc analysis was performed using Dunn’s all pair wise test. There was a significant effect of treatment (p=0.0001), but not day on OTase levels. The OTase levels ng/ml [median (quartiles)] by group were: control [4.9 (2.7, 14.1)], Preg [8.8 (6.0, 19.6)], Oxy [3.0 (0, 8.9)], and Carb [0 (0, 0)]. Oxytocin and carbetocin treated mares had the lowest OTase serum levels, and carbetocin administration lowered OTase serum to below detection limit. The regulation of OTase activity in serum requires further investigation, however it can be speculated that the changes in OTase activity are due to treatment.

Keywords: Oxytocinase, pregnant, carbetocin, oxytocin, serum