Research Report

Evaluation of an equine multi-antigen rabies combination vaccine in pregnant mares

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Abstract

Mares are commonly vaccinated during pregnancy, especially in the late third trimester, with multiple vaccine products containing a variety of antigens. Currently, a new core antigens vaccine containing rabies virus, tetanus toxoid, eastern equine encephalomyelitis virus, western equine encephalomyelitis virus, and West Nile virus with and without the inclusion of Venezuelan equine encephalomyelitis virus is used in later term mares. Use of this vaccine has not been evaluated for safety in pregnant broodmares. We determined the safety of this vaccine in pregnant mares as it pertains to live foaling rate and per cycle pregnancy rate. Findings indicated that the use of a new multi-antigen rabies combination vaccine had no impact on live foaling rate nor per cycle pregnancy rates.

Keywords: Broodmares, pregnancy, vaccination, rabies, live foaling rates, per cycle pregnancy rates

Introduction

It is a common management practice to immunize mares in late pregnancy in an effort to have adequate antibody concentrations in colostrum for passive transfer to the newborn foal and to provide disease protection for the mare. The American Association of Equine Practitioners (AAEP) recommends this practice in their vaccination guidelines.[1] Many vaccine products used for this purpose do not carry a USDA 'safe for use in pregnant mare' label claim. One common vaccine antigen used in pregnant mares for this purpose is the rabies virus. When this study was initiated, none of the rabies vaccines approved for use in horses carried a pregnant mare safety claim.[2–7] The most recently approved rabies vaccines for use in nonpregnant horses include 2 products: Core EQ Innovator™ (Zoetis, Parsippany, NJ) that includes killed rabies virus, tetanus toxoid, eastern equine encephalomyelitis (EEE) virus, western equine encephalomyelitis (WEE) virus, and West Nile (WN) virus; and Core EQ Innovator + VEE™, Zoetis (Parsippany, NJ) that is similar to Core EQ Innovator™ and also includes Venezuelan equine encephalomyelitis (VEE) virus. It is common in southern US states, especially those bordering Mexico, to include VEE in their vaccination programs. These products differ from other combination equine vaccines in that they contain all of the core equine disease antigens; rabies virus, tetanus toxoid, EEE virus, WEE virus, and WN virus as prescribed in AAEP vaccination guidelines.[1] Although rabies vaccines are frequently used in pregnant mares, there has been no objective safety evaluation for this purpose. Due to the core antigens combination in these vaccines, their relatively recent entry into the equine market and their common use in pregnant mares, a retrospective evaluation was initiated to determine the safety of these products in pregnant mares as it pertains to live foaling rate. A similar retrospective evaluation was used previously to assess the safety of an equine vaccine in pregnant mares.[8] Objectives were to determine the effects of a multi-antigen rabies combination vaccination, with and without the inclusion of VVE virus antigen, on live foaling rate in broodmares, and per cycle pregnancy rate.

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Materials and methods

For this study the definition of 'live foal' was a foal that is delivered and is able to rise and nurse on its own. Any foal not meeting this definition was counted as a 'dead foal'. Also, any pregnancy loss for any reason after administering the core antigens vaccines was also counted as a dead foal. Live foaling rate was defined as the number of mares delivering live foals/number of mares diagnosed in foal prior to receiving their normal regimen of late pregnancy vaccinations. Live foaling rate was calculated for the year prior to incorporating the core antigens vaccines (multi-antigen rabies virus, tetanus toxoid, EEE virus, WEE virus, WN virus ± VEE virus combination vaccine) in their pregnant mare populations and for the year after the use of the core antigens vaccines.

Breeding, foaling, and vaccination records of pregnant mares from 4 farms and a veterinary practice (referred to as 'Farm 4') in various areas of the country were reviewed. Two farms (Farm 1 and 3) provided data sets to determine per cycle pregnancy rate (a parameter used to evaluate reproductive efficiency[9,10]) before and after incorporating core antigens vaccines. In Farm 3, core antigens vaccination was given on a fixed date (July 21) to pregnant mares. Consequently, these mares would have been in their first or second trimester, depending upon their respective successful breeding dates. In all other data sets, the average time of vaccination was 29 days +/- 14 days of mares' calculated foaling date. These mares received additional vaccine boosters in their third trimester; however, these vaccines did not contain a rabies virus antigen.

Table 1. Live foaling rate for mares before and after receiving core antigens vaccine without VEE virus

		Pregnant mares/live foals	Live foaling % (least square means)	p
Farm 2a				
	Year before	36/33	91.85	0.5413
	Year after	60/57	95.06	
Farm 2b				
	Year before	37/34	92.08	0.6838
	Year after	52/49	94.35	
Farm 3				
	Year before	101/94	93.20	0.7830
	Year after	101/95	94.18	
Farm 5				
	Year before	195/177	91.72	0.5100
	Year after	211/196	93.41	

Table 2. Live foaling rate in mares before and after receiving core antigens vaccine containing VEE virus (note: Farm 4 data did not converge, LS Means for year after was 100% with small sample size therefore, no statistical analysis could be completed)

		Pregnant mares/live foals	Live foaling % (least square means)	p
Farm 1				
	Year before	56/53	94.71	0.3853
	Year after	83/81	97.61	
Farm 4				
	Year before	33/30	90.90	
	Year after	10/10	100	

In all, records from 975 Thoroughbred and Quarter Horse broodmares of varying age and parity were evaluated. Of which, 458 mares had data for the year before incorporating core antigens vaccines with or without VEE virus and 517 mares had data for the year after the farms began using these vaccines. Within these data, there was a subset of 370 mares that had data for 2 consecutive years for this evaluation. It was ascertained from participating farms and attending veterinarians that no substantial changes were instituted at these farms regarding feeding, husbandry, and breeding or other management practices for these 2 years.

Data analyses

Live foaling rate was determined for each farm individually and for all farms collectively. Live foaling rate was defined as a binary variable (1 = yes, 0 = no) and was analyzed by a generalized linear mixed model approach for repeated measures. Using SAS Proc Glimmix procedure (SAS 9.4, Cary, NC) combined live foaling rate of farms was analyzed with a model that considered time (before or after) as a fixed effect and farm and residual error as random effects. Animal ID-within-farm was the subject and time was the repeated factor. Covariance structure in the repeated measures analysis was investigated using compound symmetry, first-order auto-regression and unstructured model. The assumption that gave the minimum value of the Akaike's information criterion was selected in the final analysis. Analyses utilized a binomial error and logit link. Treatment least squares means were compared by two-sided t-test. The 5% level of significance was used to assess differences and for comparison of least square means. Analyses by farm were performed in a similar manner with only residual error as random effect.

Results

There were no differences ($p > 0.05$) in live foaling rate before and after incorporation of core antigens vaccines with or without VEE virus among farms individually or collectively (Tables 1–3). Live foaling rate was not different ($p > 0.05$) in the subset of 370 mares for which there were data for 2 consecutive years (Table 4). There were no differences ($p > 0.05$) in per cycle pregnancy rate before and after the incorporation of core antigen vaccines with or without VEE virus in 2 farms (Table 5).

Discussion

Breeding operations routinely use a number of vaccines containing a wide variety of antigens for pregnant mares. Vaccine antigens used in broodmares studied varied from operation to operation. At a minimum, these antigens included rabies virus, tetanus toxoid, EEE virus, WEE virus, WN virus, equine influenza virus, and equine herpes virus type I and 4. Some farms also utilized VEE virus, rotavirus, botulism toxoid, Potomac horse fever, autogenous salmonella, and autogenous

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Table 3. Live foaling rate in mares before and after receiving core antigens vaccines with or without VEE virus on all farms

	Pregnant mares/live foals	Live foaling % (least square means)	p
Year before	458/421	91.17	0.1396
Year after	517/488	94.53	

Table 4. Live foaling rate in 370 mares before and after receiving core antigens vaccines with or without VEE virus for 2 consecutive years

	Pregnant mares/live foals	Live foaling % (least square means)	p
Year before	370/341	92.81	0.5705
Year after	370/345	93.82	

Table 5. Per cycle pregnancy rate from farms 1 and 3 before and after receiving core antigens vaccine with or without VEE virus

	Number of mares	Per cycle pregnancy rate (least square means)	p
Year before	141	1.23	0.6645
Year after	159	1.21	

Clostridium difficile antigens. These vaccine antigens represented varied products and manufacturers. The only variable in the farms studied was the incorporation of the multi-antigen rabies combination vaccine that replaced the same antigens previously used but were now in a single-dose vaccine formulation. Results indicated that the new core antigen vaccines with and without VEE virus had no impact on live foaling rates. Broodmare populations on any given farm may vary from year to year. This can be due to a number of factors that include: retiring older broodmares from the herd, retiring mares due to disease or injury, death of individual mares, sale of mares, purchase of new mares and bringing young or maiden mares into broodmare populations. Breeding and foaling records evaluated included broodmares that were and were not present on farms for 2 consecutive years of this study. This was done to attain as complete an evaluation of the vaccine as possible, while emulating the normal turnover of mares within a breeding operation. It is noteworthy that there was a numerical increase (although not significant) in live foaling rate after incorporating the new vaccines.

Per cycle pregnancy rate is a parameter that can be used to evaluate breeding efficiency. Although there were no differences in per cycle pregnancy rate, during the 2 years that were evaluated, it is acknowledged that stallion fertility might have had an impact. Findings indicated that incorporation of new core antigens vaccines had no impact on live foaling rate or per cycle pregnancy rate; however, these results do not constitute a safety claim for use in pregnant mares.

Conclusion

There were no differences in live foaling rate nor per cycle pregnancy rate after incorporating the core antigens combination vaccines with and without VEE virus. Note: Since study completion, these multi-antigen rabies combination vaccines with and without VEE virus have received the following label claim: 'use of 1 dose is safe during the third trimester of pregnancy in mares' from the USDA.

Conflict of interest and funding

Senior author (Kenton Morgan) and Deborah Amodie are employees of Zoetis.

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