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Renal Papillary Necrosis in Equines

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Renal papillary necrosis (RPN) has been shown to be associated with acute pyelonephritis, urinary tract obstruction, diabetes and recently analgesic abuse. The lesion occurs in humans (Goldberg 1982; Hepinstall 1974; Kincaid-Smith 1967), rats (Murray et al. 1972), pigs (Berthe et al. 1981), horses (Gunson 1983), cattle, sheep, goats and dogs (King personal communication). Epidemiologic evidence in humans has shown that RPN due to analgesic abuse has been steadily increasing over the past thirty years (Ganong 1979). RPN has been reported to occur as an incidental lesion at necropsy that was not recognized clinically (Ganong 1979; Hepinstall 1974).

MATERIALS AND METHODS

The necropsy records of all horses necropsied at the New York State College of Veterinary Medicine (NYSCVM) Post-mortem Service between May, 1977 and February, 1983 were examined (total of 1,871) for RPN. The horses which had been treated at the NYSCVM Large Animal Clinic just prior to death (1,152) were subjected to a retrospective case controlled study. Only these horses were included in the study because good records of drug administration were necessary. Thirty of the 1,152 horses (2.6%) had RPN.

All of the affected horses records were examined for the administration of phenylbutazone (Bute) and/or flunixin meglumine (Banamine). A computer-generated random sample of 177 horses were selected from the other 1,122 clinic animals which did not have RPN. The randomly selected control horses were then categorized into a 2x2 table for prior drug administration. The table and relative risk of develping RPN after Bute and/or Banamine administration were generated as described in Mausner and Bahn (1974). The calculated Chi-square value for the odds ratio was calculated as described in Steel and Torri (1960).

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RESULTS AND DISCUSSION

Twenty-five of the thirty affected horses all had received Bute and/or Banamine with most of them getting both. Only 41 of the 177 controls received either of the drugs. The relative risk of horses developing RPN after treatment with these non-steroidal anti-inflammatory drugs was 16.6. The Chi-square value was 159.9 which at 1 degree of freedom was significant at $p<0.001$.

This study reports for the first time in veterinary literature a highly significant correlation between renal papillary necrosis and Bute or Banamine administration. Most of the affected animals that received the drug in this study received both Bute and Banamine and the number of animals receiving one or the other was too small to allow for a statistical breakdown of Bute vs. Banamine vs. the combination.

As both drugs inhibit prostaglandin synthesis and it has been shown in other species that prostaglandins are important for maintaining medullary blood flow (Rosenkrantz et al. 1981), it is possible that the combined dosing of these drugs is creating an overdose. As these drugs have never before been proven to be associated with RPN in horses, no minimum toxic dosage for causing this lesion has been reported.

Almost 50% of the affected horses had a history of dehydration or of needing fluids to maintain hydration. It is possible that horses, like rats (Nanra & Kincaid-Smith 1970), are more susceptible to developing RPN when they are dehydrated. It is also possible that as this lesion develops, urinary output increases as in other species (Murray et al. 1972) and the horses were unable to keep up with the higher fluid losses.

In humans this condition is found after long term, large dose use of non-steroidal analgesics. In this study the measurements of whether the animals received Bute and/or Banamine were limited only to the last visit which ended in the animals termination. This time period was from two days to two months, which is far short of the years it takes in people.

The short time of exposure, the high relative risk and very high significance levels suggest that these drugs have a profound effect on the equine kidney. In people, if the lesion is caught early enough, it will resolve in a large number of cases simply by stopping the analgesic (Goldberg 1982). If this also occurs in horses, not looking further back in the history should not bias the results. The relative risk for all the major breeds affected, the sex of the animals and the age of the animals was calculated and no significant increase in risk for any of those parameters was found. This supports the theory that some healing does occur, as most horses receive these drugs some time in their life. In the 41 horses which had RPN and did not receive Bute and/or Banamine in their last visit to the Large Animal Clinic, it is possible that they received the drugs before getting here and not

enough time elapsed before their death for the lesion to resolve.

Nineteen percent of the affected horses did have evidence of kidney dysfunction (elevated blood urea nitrogen or creatinine levels). That, along with 50% being dehydrated or needing fluid support, suggests that perhaps we should begin to recognize a syndrome of horses on non-steroidal anti-inflammatory agents which have trouble maintaining hydration and may or may not have other renal disease.

A series of good controlled studies are needed to determine how much of these drugs cause RPN, what predisposing factors are involved, how acutely does the lesion develop, how quickly does it resolve and how quickly (and by what means) can we clinically diagnose it,

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