Analysis of papers

Suggested format: 24.4.2007

I-Objective summary of the paper

- Less than 400 words
- What is presented, demonstrated…

II-Subjective analysis: your opinion

- Purpose of the paper
    - Originality
    - References
- Material & Methods
    - Adequacy to purpose
- Results
    - What is new?
- Discussion
    - Protocol, results…

III-Synthesis

- Why this paper has been chosen?
    - Interest
    - References
- Scientific value
    - Is the paper bringing new information?
    - Strength
    - Weakness
- What should have been done
    - To improve the paper

- What should be done in the future
    - To improve knowledge

Evaluation of the diffusion of corticosteroids between the distal interphalangeal joint and navicular bursa in horses

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1. Objective Summary

This study looks at the diffusion of two clinically utilized corticosteroids between the distal interphalangeal joint (DIPJ) and the navicular bursa (NB). Methylprednisolone acetate (MPA) and triamcinalone acetonide (TA) were used to evaluate whether clinically effective concentrations of their metabolites could be achieved by simple diffusion between the DIPJ and the NB, but studies have determined that drugs will diffuse between these structures based on factors such as physical characteristics, molecular weight and time. Its has been reported that resolution of lameness for greater than two months due to “navicular disease” was achieved for 60% of horses with NB injections versus 34% of horses that had DIPJ injection with the same corticosteroid. The degree and duration of clinical effects of injections between sites may be dose dependant or due to diffusion properties.

Thirty-two horses were divided into four groups with injections of 40mg of MPA or 10mg of TA into either the DIPJ or NB. Phase One determined the time of maximal diffusion of methylprednisolone or triamcinalone from the DIPJ to the NB or from the NB or from the NB to the DIPJ. Phase Two consisted of collection of synovial fluid samples to determine the concentrations of drug metabolites in either the DIPJ or NB at the time of maximal diffusion. Centesis of the NB was verified utilizing radiographic contrast techniques. DIPJ injection of the dorsal pouch was confirmed by synovial fluid in the needle hub. Dilution techniques, with sterile saline and MPA or TA, were utilized that would allow for adequate synovial fluid collection for sufficient calculations of concentration assays. Serum was collected for urea concentration for later comparison and dilution factor concentration determinations of synovial samples. Synovial fluid samples were analyzed for MPA or TA, and their metabolites, by use of established high-performance liquid chromatography methods. Data analysis took into account dilution factors during collection of synovial samples and determined diffusion quantity standardized to a milligram-per-milligram basis of corticosteroids injected.

Results of Phase One showed a peak diffusion time of three hours after injection for all four groups. Phase Two measured the specific concentration of drug metabolites within the synovial structures following diffusion of three hours. Product injected (MPA or TA) had no significant effect on rate of diffusion of metabolites, but there was a greater corticosteroid metabolite diffusion when the DIPJ was injected. Diffusion of methylprednisolone and triamcinalone from the DIPJ was not different, but triamcinalone diffused nine times more readily from the NB than methylprednisolone.

The discussion section of this study centered on numerous aspects related to clinical practice. The doses of MPA and TA used for injection delivered a clinically effective anti-inflammatory concentration following diffusion to either the DIPJ or NB, based on data for minimum effective concentration. Higher concentrations of the

metabolites may be obtained by higher doses of corticosteroids or by diffusion into a smaller amount of synovial fluid. There was discussion about diffusion of metabolites in other joints and how rates of diffusion and concentration levels may vary due to physiologic aspects of specific joints and the doses of the drugs utilized. Results of this study suggest that the drugs MPA and TA injected into the DIPJ can achieve clinically effective concentrations of their active metabolites in the NB by way of diffusion.

II. Subjective Analysis

1. Purpose of this paper

   The originality came from performing this study between the DIPJ and the NB. Similar work, as a model, had been done with the carpal and tarsal joints. This report utilized synovial structures, but I believe there are likely some subtle differences between the bursal and joint synovial structures metabolically.

2. Materials & Methods

   There was great effort to obtain clean, correct samples for analysis. Radiographic and contrast material assistance for sampling was utilized. Adequate break periods were allocated for withdrawal of drugs prior to subsequent testing. Dilution and concentration correction factors were utilized. I believe the results of the concentration values were well substantiated and validated.

3. Results

   The diffusion of the medications is adequate in either direction from the DIPJ to NB or NB to DIPJ and they can attain clinically effective concentrations.

This is useful information for the practitioner because the DIPJ is more easily accessible with potentially less problems from the injection techniques.

4. Discussion

I think this section addressed a number of factors that have importance in clinical practice. The minimum effective anti-inflammatory concentrations of methylprednisolone and triamcinalone were achievable with the doses used in this study and those used in clinical practice. Factors that influence the minimum effective or therapeutic concentration and duration action, such as potency of corticosteroids, binding affinity, rate of hydrolysis, total dosage, diffusion rates and individual variation in animals, were discussed adequately.

III. Synthesis

1. Why paper was chosen

Navicular bursa injections are more challenging and, I believe, have more potential for future harmful consequences. It would be nice to have a way to deliver effective drug concentrations into the bursal area with an easier technique. This report supports the idea that treating the DIPJ will get effective levels into the NB. A comment in the discussion section hints that treating the DIPJ with a higher dose of corticosteroids will give a higher concentration of the metabolite in the NB and possibly a better therapeutic effect.

2. Scientific Value

I believe the study gives more validity to the idea that this whole region and apparatus works as a unit and there is a lot of interaction between structures. Treatment of one area is treating other structures as well.

3. What should have been done

Overall, I believe the study was well conceived and carried out.

4. What should be done in the future

- Possible lameness model of either DIPJ or NB and then use treatment in the other structure to see if it would be effective. Could possibly determine a measurable effective concentration, of different drugs, within synovial fluid for the model.
- Use different injection doses to determine if diffusion rates or concentrations of metabolites, between or within these synovial structures, develop some dose-related patterns that may eventually play a role in clinical effectiveness.