Safety Study on the Effects of Intra-articular Polyglycan at 1X and 3X Doses

CE Kawcak DVM, PhD, Diplomate ACVS
Associate Professor, Equine Orthopaedic Research Laboratory, Colorado State University

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The goal of this study was to evaluate the safety of Polyglycan at 1X and 3X doses, compared to saline controls and untreated joints using the equine middle carpal joint. Since the 1X dose needed to be evaluated at doses administered once weekly for 3 weeks, and the 3X dose only once over 7 days, the study was divided into 2 sets of analyses. 8 horses were used per group for a total of 24 horses, and one middle carpal joint served as the treated joint, randomly assigned either placebo, 1X Polyglycan or 3X Polyglycan. The opposite middle carpal joint served as an untreated control. All horses were evaluated for lameness, synovial effusion and response to joint flexion on days 0 (before treatment) and day 7. Synovial fluid was sterilely aspirated from each middle carpal joint from each horse on days 0 (before treatment administration), 1, 3, 5 and 7. At this point, the horses treated with 3X Polyglycan were released from the study, and the remaining 16 horses completed the 21 day portion of the study. Lameness examinations were again performed on days 14 and 21. Synovial fluid was aspirated on days 14 (before treatment administration) and again on day 21.

Data analysis was divided into 2 parts. In the first analysis (Analysis A) the effects of control, placebo, 1X Polyglycan and 3X Polyglycan were compared using a Repeated Measures Analysis of Variance between days 0 and 7. The dependent variables were lameness, synovial effusion, response to joint flexion, synovial fluid WBC and Total Protein. $P<0.05$ was considered significant. In the second analysis (Analysis B) the effects of control, placebo and 1X polyglycan were compared using the same methods between days 0 and 21.

Results

The safety study yielded no adverse effects in clinical observations of the patients. There was no evidence of lameness, synovial effusion or painful response to joint flexion noted in the administration of Polyglycan.

In Analysis A, synovial fluid WBC increased significantly on day 1 (24 hours after initial aspiration) in all groups (Figure 1). In addition, synovial fluid WBC was significantly higher in the middle carpal joints of placebo, 1X and 3X treated horses compared to untreated control on day 1, but this decreased significantly from day 1 on days 3, 5 and 7, resulting in no significant difference from control at these days (Figure 2). The same was true for synovial fluid total protein, as it too increased significantly on day 1 in all groups (Figure 3) and increased significantly on day 1 in all 3 treatment groups compared to untreated control (Figure 4). The same was true for Analysis B, namely, that WBC increased significantly on day 1, then decreased over time, and WBC was significantly higher in treated joints compared to control at day 1 (Figure 5). In addition, the same was true for synovial fluid Total Protein, in that it too increased at day 1, however, there was no significant treatment-by-study day interaction, and for pooled treatment data, placebo remained significantly higher than control over the duration of the study (Figure 6).

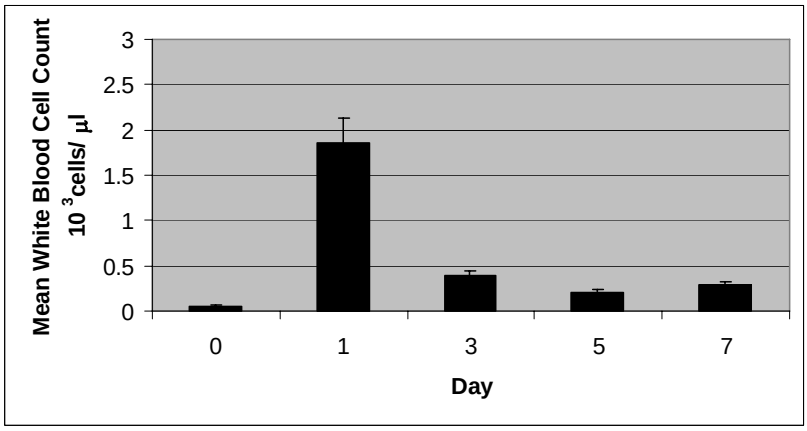

Figure 1. Mean and standard error of white blood cell counts in synovial fluid on day 0, 1, 3, 5, 7 (pooled over treatment groups).

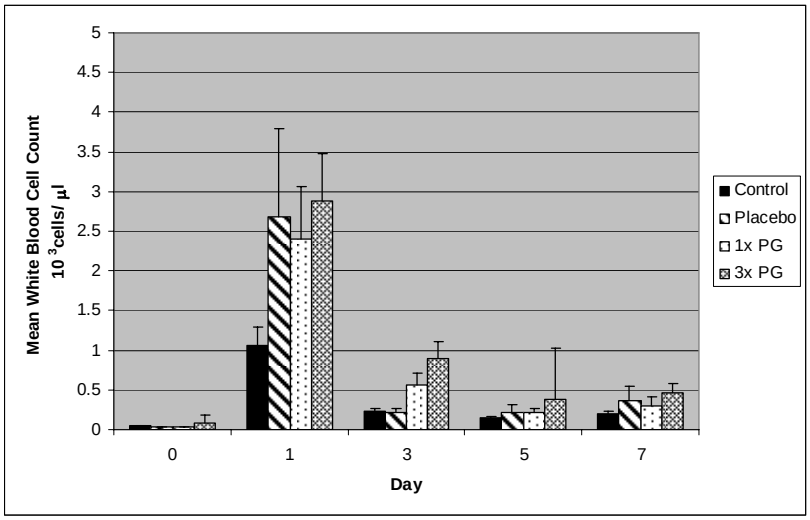

Figure 2. Mean and standard error of white blood cell counts in synovial fluid on day 0, 1, 3, 5, and 7 for the control, placebo, 1x and 3x groups.

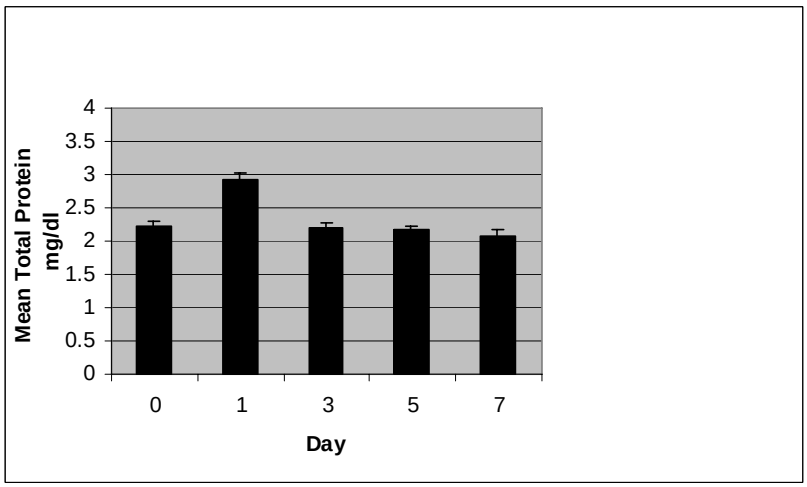

Figure 3. Mean and standard error of Total Protein in synovial fluid on days 0, 1, 3, 5 and 7 (pooled over treatment groups)

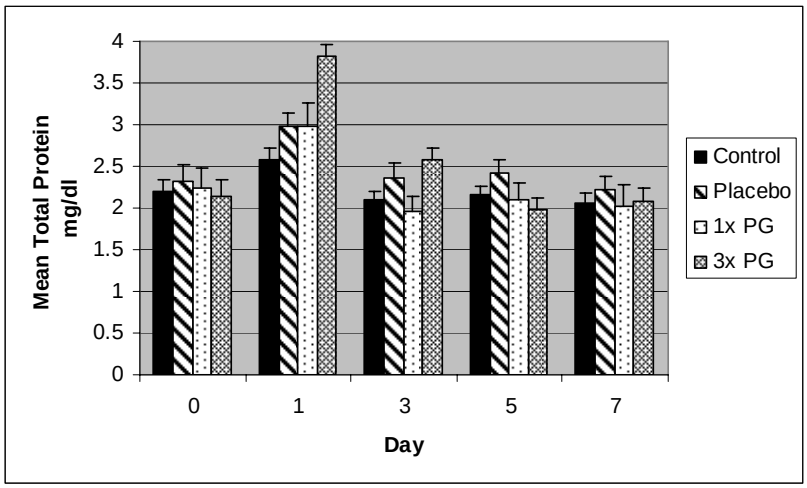

Figure 4. Mean and standard error of Total Protein in synovial fluid on day 0, 1, 3, 5, and 7 for the control, placebo, 1x and 3x groups.

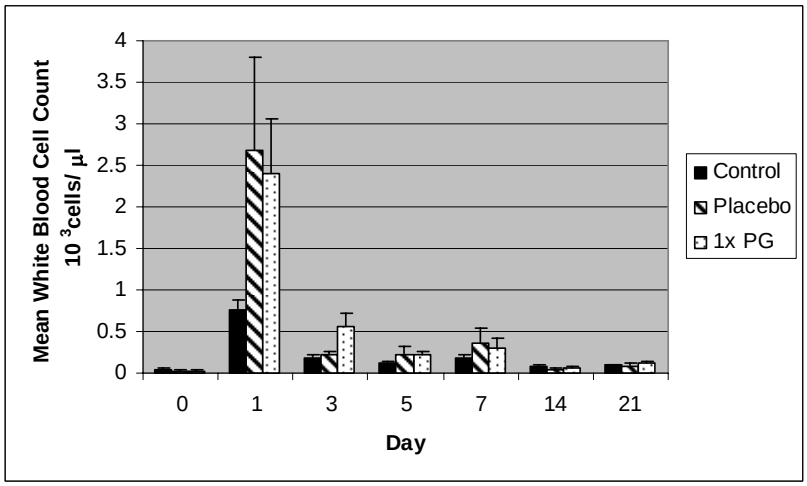

Figure 5. Mean and standard error of white blood cell counts in synovial fluid on day 0, 1, 3, 5, 7, 14 and 21 for the control, placebo, and 1x groups.

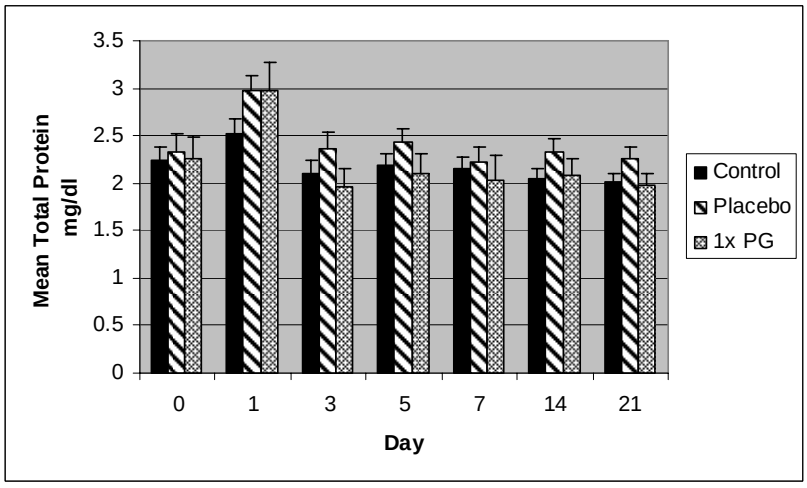

Figure 6. Mean and standard error of Total Protein in synovial fluid on day 0, 1, 3, 5, 7, 14 and 21 for the control, placebo, and 1x groups.

It appears that there were no detrimental effects of Polyglycan administered at 1X dose once a week for 3 weeks, or Polyglycan administered at 3X dose once when compared to intra-articular placebo injection. There were no effects on clinical parameters, and those changes in synovial fluid parameters were reflective of fluid administration, including saline as a placebo.