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Summary

Reasons for performing study: There is a lack of long-term follow-up data for outcome of medical treatment of superficial digital flexor (SDF) tendonitis.  
Objectives: To determine whether intralesional injection of hyaluronan, beta aminoproprionitrile fumarate (BAPN) or polysulphated glycosaminoglycans (PSGAG) or systemic administration of PSGAG yielded better results than a controlled exercise programme alone in the management of SDF tendonitis, with a minimum follow-up period of 2 years after resumption of full work; and to determine whether reinjury rate was related to sports discipline and whether fibre alignment score (FAS) at 4 months could predict outcome.  
Methods: In Study 1, 50 horses were managed by controlled exercise alone (Group A), 50 were treated with intralesional injection of hyaluronan (Group B), 20 received intralesional and systemic treatment with PSGAG (Group Ci) and 30 received systemic treatment with PSGAG (Group Cii). Horses in Groups B, Ci and Cii followed the same controlled exercise programme as Group A. In Study 2, 69 horses (Group D) were treated by intralesional injection of BAPN and followed a modified controlled exercise programme. Horses were re-examined clinically and ultrasonographically at intervals. Follow-up data were obtained for horses 2 years after resuming full work and for up to 6 years.  
Results: There was no significant difference in reinjury rate of the treated limb(s) between Groups A, B, Ci and Cii (42.5–44.4%) (P>0.9). The reinjury rate (16%) in the treated limb(s) in Group D was significantly lower than in the other groups (P<0.001). However, when injury rate of the uninjured limb was considered, the results were similar to Study 1. In Study 2, the FAS at 4 months after treatment was a good predictor of outcome (P<0.001). Reinjury rates for different disciplines were similar in the 2 studies, with the risk of reinjury ascending from showjumpers to event horses to National Hunt and flat racehorses.  
Conclusions: Treatment with BAPN reduced the risk of reinjury in the treated limb, although the overall rate of subsequent injury was not affected. FAS at 4 months after treatment is a good predictor of outcome in the treated limb(s).  

Potential relevance: This study provides long-term follow-up data in horses from a variety of sports disciplines that can be used to provide prognostic information.

Introduction

Superficial digital flexor (SDF) tendonitis is a potentially career-limiting injury, with a high incidence of reinjury (Genovese et al. 1996; Palmer et al. 1994; Yovich et al. 1995). Most of the published data relating to SDF tendonitis relate to Thoroughbred flat (Genovese et al. 1996; Gibson et al. 1997) and National Hunt (Marr et al. 1993; Ordidge 1996) racehorses and Standardbred racehorses (Hawkins and Ross 1995). There are limited data concerning other disciplines (Palmer et al. 1994; van den Belt et al. 1994; Dyson 1998). However, SDF tendonitis is important in other sports horses, especially event horses (Palmer et al. 1994; Gibson et al. 2002; Bathe 2003; Dyson 2003) and Grand Prix showjumpers (Palmer et al. 1994; Boswell et al. 2003; Dyson 2003). Long-term follow-up information for nonracing sports disciplines is lacking.

Experimental studies using a collagenase-induced tendonitis model have investigated the effects of intralesional injection of hyaluronan (Spurlock et al. 1989; Gaughan et al. 1991, 1995) or beta aminoproprionitrile fumarate (BAPN) (Alves et al. 2001), or systemically administered polysulphated glycosaminoglycan (PSGAG) (Redding et al. 1992). There are limited published data relating to treatment of clinical cases of SDF tendonitis with hyaluronan (Hertsch et al. 1989) or PSGAG (Marr et al. 1993; Dow et al. 1996). More recently, the clinical use of intralesional BAPN was described (Genovese et al. 1996; Reef et al. 1996, 1997). The importance of controlled exercise in the management of tendonitis has also been emphasised (Genovese et al. 1996; Gillis 1997).

This paper reports 2 consecutive related studies, the first (Dyson 1997) comparing results of treatment with intralesional hyaluronan or PSGAG and systemic administration of PSGAG with controlled exercise alone. The second study compares the results of treatment with beta aminoproprionitrile fumarate (BAPN) in 69 horses with those of the previous study.

The purposes of these studies were to: 1) compare the reinjury rate in horses treated by controlled exercise alone, or in combination with either intralesional treatment with hyaluronan, PSGAG or BAPN or systemic administration of PSGAG, with a minimum follow-up period of 2 years after return to full work; 2) determine whether outcome could be predicted by ultrasonographic

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determination of fibre alignment grade; and 3) compare reinjury rates in horses from different disciplines.

Materials and methods

Horses were selected for inclusion in the study by clinical and ultrasonographic evidence of forelimb SDFT tendinitis, either unilaterally or bilaterally. Horses with first-time or recurrent injuries were included. All horses were examined ultrasonographically bilaterally using a 7.5 or 10 MHz transducer. The cross-sectional area (CSA) of the SDFT was measured at 4 cm intervals distal to the accessory carpal bone (ACB), and an echogenicity score (0–3) assigned (Rantanen et al. 2003). Fibre alignment score (FAS) (Rantanen et al. 2003) was assessed in longitudinal images and the grade (0–3) refers to the score at the cross-sectional area of the tendon which appeared abnormal ultrasonographically.

Study 1

Horses in Study 1 (n = 150) were examined over 2 years from 1992 to 1994 (Dyson 1997). Fifty horses (Group A) were treated conservatively and owners were advised to follow a controlled exercise programme (Table 1). Fifty horses (Group B) were treated by intralesional injection of high molecular weight hyaluronan (Hylar�vit Vet)1. Twenty horses (Group Ci) received intralesional PSGAG (Adequan2) (500 mg) and 7 i.m. injections of PSGAG at 5 day intervals. Thirty horses (Group Cii) received 7 i.m. injections of PSGAG at 5 day intervals. Both limbs were treated in Group A. It was recommended that horses should not start cantering exercise until 12 to 16 months after injury, depending on the ultrasonographic appearance of the tendons.

It was not possible to assign all horses randomly to treatment groups due to lack of client compliance. The population of each group was mixed, given the variability of lesion severity, number of limbs affected and discipline for which each horse was used. An attempt was made to have similar proportions of horses from each discipline in each treatment group, and to assign horses to treatment groups irrespective of the severity of injury.

Horses were examined clinically and ultrasonographically at approximately 3 month intervals after treatment, until 12 to 15 months after treatment. Follow-up information was obtained at 2 years after each horse started cantering, or sooner if re-injury had already occurred. The results are based only on those horses (135) that returned to their former athletic function.

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### TABLE 1: Guidelines for the controlled exercise programme in Study 1 (progress was guided by ultrasonographic appearance of the tendons whenever possible)

<table>
<thead>
<tr>
<th>Weeks</th>
<th>Duration and nature of exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–4</td>
<td>15 mins walking exercise in hand twice daily</td>
</tr>
<tr>
<td>4–8</td>
<td>45 mins walking in hand, on horse-walker or ridden</td>
</tr>
<tr>
<td>8–12</td>
<td>60 mins walking in hand, on horse-walker or ridden</td>
</tr>
<tr>
<td>16–24</td>
<td>Turn-out in small paddock and ridden walking exercise with short periods of trot, for 60 mins</td>
</tr>
<tr>
<td>24–48</td>
<td>Turn-out in large paddock and ridden walking and trotting exercise, with progressive increase in duration of trot</td>
</tr>
<tr>
<td>48–52</td>
<td>Flat work, walk and trot</td>
</tr>
<tr>
<td>52</td>
<td>Ridden walk, trot and canter</td>
</tr>
</tbody>
</table>

Table from Dyson (1997).

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### TABLE 2: Distribution of horses for which follow-up was available among treatment groups in Study 1

<table>
<thead>
<tr>
<th>Disciplines</th>
<th>Study 1</th>
<th>Study 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group A</td>
<td>Group B</td>
</tr>
<tr>
<td>R(F)</td>
<td>2</td>
<td>4.3</td>
</tr>
<tr>
<td>R(NH)</td>
<td>13</td>
<td>28.2</td>
</tr>
<tr>
<td>E</td>
<td>23</td>
<td>50.0</td>
</tr>
<tr>
<td>SJ</td>
<td>4</td>
<td>8.7</td>
</tr>
<tr>
<td>End</td>
<td>2</td>
<td>4.3</td>
</tr>
<tr>
<td>Dr</td>
<td>2</td>
<td>4.3</td>
</tr>
<tr>
<td>Total</td>
<td>37</td>
<td>74</td>
</tr>
</tbody>
</table>

*R(F) = Flat racing; R(NH) = National Hunt racing; E = Eventing; SJ = Showjumping; End = Endurance; Dr = Dressage. Table modified from Dyson (1997).

Study 2

Horses in Study 2 (n = 69) were examined between July 1996 and May 2000 (the study is still ongoing, but results are presented only for horses for which follow-up information for at least 2 years after resuming full work was available). Horses were selected based upon ultrasonographic evidence of SDF tendinitis with a CSA of the tendon at maximum injury site of >1.5 cm² and/or a hypoechogenic region occupying >50% of the CSA of the tendon and extending more than 1.5 cm proximodistally. Treatment was not performed until at least 4 weeks after injury.

Horses were treated by intralesional administration of 7–18 mg BAPN3, depending on the length of the lesion. Multiple injections were performed using a 27 gauge needle on 5 occasions on alternate days. Injections were performed with the limb bearing weight and with the horse sedated using detomidine and butorphanol. Injections extended proximal and distal to the region of tendon which appeared abnormal ultrasonographically.

Seventeen horses were treated bilaterally and 52 unilaterally. Horses were walked for 30 mins daily on a horse-walker throughout the treatment period and, for the following 4 months, walking exercise was continued for up to 45 mins in hand, on a walker or ridden. In the early phase of the trial, short periods of trotting exercise were introduced after 8 weeks, but this appeared to be detrimental (resulting in swelling and lameness in some cases).

Horses were re-examined clinically and ultrasonographically 4 months after treatment and at variable intervals thereafter, depending on clinical progress. Subsequent exercise management was dependent on the ultrasonographic appearance of the tendon. Most horses were back in moderate cantering exercise by 12 months after injury. In Study 2, follow-up data were assessed for 68 horses that had been back in full work for at least 2 years and up to 6 years (to May 2003).

Statistical analysis

Chi-squared analysis was used to assess differences in reinjury rates between treatment groups in Study 1 and between Studies 1 and 2. The effect of discipline and fibre alignment score on reinjury were tested using Fisher’s Exact test.

Results

In both studies, the injections were well tolerated. No adverse reactions to injection were seen. In Study 2, injections extended proximal and distal to the site of lesions detected...
TABLE 3: Incidence of recurrent injury in horses which returned to their former athletic function related to treatment group and discipline in Study 1

<table>
<thead>
<tr>
<th>Discipline</th>
<th>Group A</th>
<th>Group B</th>
<th>Group Ci</th>
<th>Group Cii</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. %</td>
<td>No. %</td>
<td>No. %</td>
<td>No. %</td>
</tr>
<tr>
<td>R(F)</td>
<td>1/1 100</td>
<td>1/2 50</td>
<td>0/0 0</td>
<td>0/0 0</td>
</tr>
<tr>
<td>R(NH)</td>
<td>5/10 50</td>
<td>4/7 57</td>
<td>2/4 50</td>
<td>3/4 75</td>
</tr>
<tr>
<td>E</td>
<td>10/23 43</td>
<td>11/25 44</td>
<td>5/12 42</td>
<td>8/19 42</td>
</tr>
<tr>
<td>SJ</td>
<td>1/4 25</td>
<td>1/5 20</td>
<td>1/2 50</td>
<td>0/2 0</td>
</tr>
<tr>
<td>End</td>
<td>0/2 2</td>
<td>2/5 40</td>
<td>0/0 0</td>
<td>0/1 0</td>
</tr>
<tr>
<td>Dr</td>
<td>1/2 50</td>
<td>1/3 33</td>
<td>0/0 0</td>
<td>1/2 50</td>
</tr>
</tbody>
</table>

For abbreviations, see Table 2.

ultrasonographically. It was easy to discern whether the tendon was normal by the force of resistance to injection. Injection was easy into damaged tendon, which almost invariably extended at least 2 cm proximal and distal to the lesion detected ultrasonographically. In Study 1, client compliance with the exercise programme was less than in Study 2. Eight horses in Study 1 started cantering exercise earlier than recommended, between 10 and 12 months after treatment. The majority of horses in Study 1 (n = 118) started cantering between 12 and 14 months after treatment, whereas in Study 2 most horses (n = 66) were in moderate canter work by 12 months after treatment.

Study 1

Follow-up information was available for 140 horses (Group A, 46; Group B, 47; Group Ci, 18 and Group Cii, 29) (Table 2). Five of these horses (1 flat racehorse, 3 National Hunt racehorses and 1 event horse) did not return to their former athletic function, but were used for hunting or pleasure riding. None of these horses had recurrent injury, but they were excluded from further analysis. In the remaining 135 horses the incidence of reinjury to the treated limb(s) between groups ranged from 42.5 to 44.4% (Table 3). There was no significant difference between treatment groups (P = 0.90). There was no significant effect of discipline (P = 0.35), but there was a trend for higher incidence of reinjury in racehorses (flat and National Hunt) than in eventers and dressage horses (Table 4). Reinjury rate was lowest in showjumpers and endurance horses. The data for subsequent injury to nontreated limbs are not available.

Study 2

One racehorse was retired as a breeding stallion; data are presented for the remaining 68 horses (34 event horses, 26 racehorses, 7 showjumpers and 1 cross-country horse). The reinjury rate was significantly less (P<0.001) than in Study 1, with only 11 of 68 horses (16%) sustaining recurrent injury to a treated limb (Table 5). However, when injuries to the contralateral limb were considered in horses treated unilaterally, the injury rate was similar to Study 1, with 45.6% of horses experiencing injury. The reinjury rate for different disciplines was very similar to that in Study 1, with the risk of reinjury ascending from showjumpers to event horses to flat and National Hunt racehorses.

Event horses formed the largest discipline group (Study 1, 79 horses; Study 2, 34 horses). In Study 2 there was a higher proportion (Study 1 24/79 [30%]; Study 2 22/34 [65%]) of Advanced level event horses, competing at 3-day events up to Federation Equestre Internationale (FEI) 4-star level. In Study 1, no horse completed more than two 3-day events without recurrent injury. Fourteen horses in Study 2 completed from 2 to six 3-day events without injury. None of these horses completed 3 or more FEI 4-star events. A further 5 horses completed from 2 to five 3-day events before injuring the contralateral limb; 3 of these horses have since completed 2 further 4-star 3-day events.

There were significant differences between fibre alignment scores and reinjury (P<0.001). All 4 horses with a FAS at the MIZ of 2 or 3 at 4 months after treatment had recurrent injury of the treated limb. Seven of 30 horses with a FAS of 1 suffered reinjury, whereas no horse (n = 34) with a FAS of 0 reinjured the treated limb.

Discussion

In Study 1 there appeared to be no benefit of treatment with either hyaluronan or PSGAG compared with controlled exercise alone. In Study 2 there was a significant reduction in reinjury rate of the treated limb compared to Study 1, but when reinjury of the untreated limb was considered, the overall results were similar. However, data for injury of the untreated limb were not available

TABLE 4: Incidence of reinjury related to discipline in Study 1. Differences between disciplines were not significant (P = 0.35)

<table>
<thead>
<tr>
<th>Discipline</th>
<th>Total No. horses</th>
<th>No. horses with recurrent injury</th>
<th>% Reinjury</th>
<th>New injury to untreated limb</th>
<th>Total injury</th>
<th>% Total injury</th>
</tr>
</thead>
<tbody>
<tr>
<td>R(F)</td>
<td>3</td>
<td>2</td>
<td>66.7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R(NH)</td>
<td>25</td>
<td>14</td>
<td>56.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E</td>
<td>79</td>
<td>34</td>
<td>43.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SJ</td>
<td>13</td>
<td>3</td>
<td>23.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>End</td>
<td>8</td>
<td>2</td>
<td>25.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dr</td>
<td>7</td>
<td>3</td>
<td>42.8</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

For abbreviations, see Table 2.

TABLE 5: Incidence of reinjury to a treated limb or new injury of an untreated limb related to discipline in Study 2 in 68 horses for which follow-up data was available

<table>
<thead>
<tr>
<th>Discipline</th>
<th>Total No. horses</th>
<th>No. horses with recurrent injury</th>
<th>% Reinjury</th>
<th>New injury to untreated limb</th>
<th>Total injury</th>
<th>% Total injury</th>
</tr>
</thead>
<tbody>
<tr>
<td>R(F)</td>
<td>16</td>
<td>2</td>
<td>12.5</td>
<td>8</td>
<td>10</td>
<td>62.5</td>
</tr>
<tr>
<td>R(NH)</td>
<td>10</td>
<td>4</td>
<td>40.0</td>
<td>2</td>
<td>6</td>
<td>60.0</td>
</tr>
<tr>
<td>E</td>
<td>34</td>
<td>5</td>
<td>14.7</td>
<td>9</td>
<td>14*</td>
<td>41.2</td>
</tr>
<tr>
<td>SJ</td>
<td>7</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>14.3</td>
</tr>
<tr>
<td>Cross country</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>68</td>
<td>11</td>
<td>-</td>
<td>-</td>
<td>31</td>
<td>-</td>
</tr>
</tbody>
</table>

*One additional horse sustained desmitis of the accessory ligament of the deep digital flexor tendon in 1 of 2 treated limbs. For abbreviations, see Table 2.
for Study 1. In both studies, reinjury was highest in racehorses; event horses were at medium risk of reinjury and showjumpers at low risk. Horses treated with BAPN returned to cantering exercise and competition earlier than the horses in Study 1, apparently without detrimental results. In Study 2, FAS at 4 months after treatment was a good predictor of outcome.

These combined studies had a number of limitations. The studies were sequential and not concurrent. The overall clinic case load did not alter with respect to discipline during the study periods, although the proportion of Warmblood breeds slowly increased, reflecting the growing use of these breeds, especially for dressage and showjumping. Treatments were neither randomised nor blinded. There was not a control group. The studies depended on client compliance with the exercise regime, which was less good in Study 1 than Study 2. Interpretation of the results is also confounded by the variety of athletic sports in which the horses were involved, severity of the initial injury, whether it was a first-time injury or reinjury, whether the injury was unilateral or bilateral, and the age of the horse. Some horses in Study 1 would not have met the lesion severity inclusion criteria for Study 2. These were selected because, in a previous study (Reef et al. 1997), there was no demonstrable benefit of BAPN treatment in mild lesions compared with controlled exercise alone. In the current studies, the horses in the treatment groups were otherwise comparable, except that there was a greater proportion of high level event horses in Study 2. However, in Study 1 data were available only for reinjury of the treated limb(s), whereas in Study 2 data were available for both reinjury and new injury of untreated limbs.

When reinjury of the treated limb is considered, there were superior results with treatment using BAPN. This is contrary to experimental data in a collagenase-induced tendonitis model in rabbit Achilles tendons in vivo (Yamamoto et al. 2002) in which BAPN appeared to inhibit healing, whereas hyaluronan promoted healing. It is also conflicts with an in vitro study investigating the effects of BAPN on normal equine tenocyte metabolism (Dahlgren et al. 2001). However, these experimental studies focused on the short-term effects of BAPN, whereas the current study investigated long-term outcome. In the current study, there appeared to be no benefit for preventing reinjury by treatment with either hyaluronan or PSGAG compared with controlled exercise. Previous experimental studies using hyaluronan have shown conflicting results (Spurlock et al. 1989; Gaughan et al. 1991; Poland et al. 1992; Gift et al. 1992; Yamamoto et al. 2002). The only other documented clinical study (Hertsch et al. 1989) had extremely short-term (3 to 10 months) follow-up data. There are 2 documented clinical trials investigating the effect of PSGAG (Marr et al. 1993; Dow et al. 1996), but the study of Dow et al. (1996) lacked reliable follow-up information. Marr et al. (1993) compared conservative management with laser treatment or intralesional or i.m. PSGAG in National Hunt racehorses with a follow-up period of 9 to 30 months. There was no significant difference in the proportion of horses returning to training in the 3 groups, but horses treated with PSGAG had a higher risk of reinjury.

This is the first documented long-term study on a large number (n = 113) of event horses and also permits comparisons with reinjury rates in horses from other disciplines. The highest reinjury rate was in flat and National Hunt racehorses. The high incidence of tendon injury and reinjury in National Hunt racehorses is well recognised (Dyson et al. 2003). Serious tendon injury in young flat racehorses in the UK is generally not regarded as a major problem (Pilsworth 2003). It is possible that the treated horses were inherently susceptible to injury, with a high proportion injuring the contralateral limb in Study 2. The new or recurrent injury rate in flat racehorses was similar to that reported in New Zealand in horses treated either conservatively or by desmotomy of the accessory ligament of the SDFT (Gibson et al. 1997). All the showjumpers were competing at Grand Prix level and in both studies had a comparatively low reinjury rate, despite being a group of higher mean age (13 years) than in any other discipline. Degenerative changes in the equine SDFT develop with age and are thought to predispose to injury (Smith 2003). The high rate of reinjury in dressage horses in Study 1 was surprising because SDF tendonitis is not a major problem in this discipline (Kold and Dyson 2003). This may also reflect an inherent susceptibility to tendon injury in these individuals. The use of BAPN enhanced the likelihood of event horses being able to complete more than two 3-day events compared to other treatment methods. Nonetheless, when injuries to the non-treated limb were considered, the overall injury rate in the follow-up period was similar in both studies, irrespective of treatment.

During the BAPN injection procedure it was clear that areas of damaged tendon extended proximal and distal to the sites identified as abnormal using ultrasonography. This highlights the potential limitations of ultrasonography. It is therefore possible in horses with unilateral injury that regions of damaged tendon in the contralateral asymptomatic limb were missed. Experience comparing ultrasonography with magnetic resonance imaging (MRI) in the distal metacarpal and pastern regions has demonstrated that tendon lesions detectable using MRI are often either not detectable or considerably smaller when assessed ultrasonographically (S. Dyson and R. Murray, unpublished data). Consideration should be given to assessment of the tendon architecture in the apparently normal limb by attempting injection into the tendon.

In Study 2, FAS at 4 months after treatment was a good predictor of final outcome, in accordance with a previous study (Reef et al. 1997). Regular ultrasonographic monitoring during the rehabilitation period was used to control changes in the exercise regime. The work programme for individual horses was based on the stability of the CSA of the tendon and its echogenicity score and FAS.

One event horse in Study 2 with bilateral injury returned to competition, but subsequently developed desmitis of the accessory ligament of the deep digital flexor tendon, a comparatively unusual injury in event horses. No horse in either study developed suspensory desmitis.

In conclusion, BAPN reduced the reinjury rate in the treated limb compared with other medical treatments; however, long-term injury rate in the untreated limb remained high. Injection of mesenchymal stem cells may result in enhanced healing (Smith et al. 2003), but requires long-term validation. Based on the results of the current study, consideration may have to be given to treatment of both limbs, even if lesions are detected in only one limb using ultrasonography.

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Manufacturers’ addresses

1Pharmacia & Upjohn Animal Health, Corby, Northamptonshire, UK.
2Janssen Animal Health, High Wycombe, Buckinghamshire, UK.
3Sigma Pharmaceuticals, Poole, Dorset, UK.

References


