Introduction

Tendon suture fixation is imperfect. Although elaborate suture techniques improve tensile strength of tendon repair, all appear to result in decreasing suture fixation some days after the operation. Studies concerning flexor or Achilles tendon repair report a (re)rupture rate of 3 to 6%. Repair-site elongation (gap formation) is much more common, resulting in slower healing and with that, poorer clinical outcome.

Matrix metalloproteinases (MMPs) are essential in tissue remodelling and act as part of the inflammatory response to clear up debris. Implantation of a foreign material into the tendon invariably evokes a tissue reaction and there is evidence of elevated MMP activity in the direct vicinity of sutures inserted into tendons.1 This probably weakens the tissue and allows the suture to cut through the tendon when exposed to tensile stress, i.e. during early mobilisation. An analogous reduction in suture holding capacity is described in animal models of intestinal anastomoses. There, systemic treatment with MMP-inhibitors can totally preserve original strength.2

We evaluated the effect of systemic doxycycline on tendon suture fixation. First, we examined the effect of systemic doxycycline. Then, doxycycline was applied locally, by using a new method for coating suture material. We hypothesised that systemic and local doxycycline treatment would improve suture pull-out strength in the rat Achilles tendon.

Methods

Systemic treatment

40 male Sprague Dawley rats weighing 405 (SD 24) g were randomised to receive deionised drinking water with or without doxycycline 80 mg/kg/day, which gives a clinically relevant serum concentration. Suture fixation was evaluated 3 days after operation.

Local treatment

A polybutester suture was coated with doxycycline hydrochloride (4 nm, Sigma) on top of EDC/NHS crosslinked fibrinogen (30 nm, Haemochrom Diagnostica). The total amount of immobilized drug was measured by ellipsometry. Regular nylon sutures served as controls.

43 male Sprague Dawley rats weighing 375 (SD 23) g were randomised to 3 groups: 16 controls and 17 rats receiving a doxycycline-coated suture were evaluated 3 days after operation. 10 more rats were evaluated immediately.

Surgical procedure and mechanical evaluation

The study was approved by the regional animal ethics committee. Animals were anaesthetised with isoflurane gas. An oblique 1 cm skin incision was made over the left Achilles tendon. A 3-0 monofilament polybutester suture with a tapered needle (Novafil, Tyco Healthcare) was inserted into the intact tendon to make a modified Kessler stitch spanning 1 cm longitudinally, starting at the tendon’s superior end 2 mm from the musculotendinous junction. Thereafter the free ends were approximated with a double knot, leaving a loop 1 cm in diameter. The Achilles tendon was then cut transversely just proximally to the suture to unload the tendon. Thus, the Kessler stitch was only inserted into the distal part of the tendon. The plantaris tendon was cut and the skin was sutured.

On the evaluation day, the tendon with the attaching calcaneus was dissected clean from surrounding tissue. The calcaneus was fixed in a clamp while the suture loop was attached to a hook via a freely movable metal device to allow a straight pull. The complex was mounted in a materials testing machine and pulled at a constant speed of 0.1 mm/s until pull-out. Peak force was recorded. The two separate studies were analysed by way of Mann-Whitney U tests. Because systemic treatment indicated a positive effect, a one-tailed test could be used for local treatment.

Results

Systemic treatment

Two rats from the control group and six rats from the doxycycline group were excluded from analysis either due to technical issues or weight loss >2SD below mean weight loss.

The suture pull-out strength was higher in the doxycycline treated tendons (median 16 N, interquartile range 14-20) as compared to controls (median 14 N, interquartile range 12-16) on the third postoperative day (p=0.025).

Locally treated tendons (median 18 N, interquartile range 16-22) showed a statistically significant improvement compared with controls. Doxycycline-coated sutures served as controls.

Discussion

Our data indicate that tendon suture fixation can be improved by treatment with an MMP-inhibitor. The size of the effect was similar with both systemic and local administration.

Local doxycycline aborted a third of the unwanted decrease in suture fixation after three days, an effect large enough to have potential clinical importance. A retained suture holding capacity mediated by an MMP-inhibitor might allow an earlier and safer start of rehabilitation programs after surgical repair of tendon rupture. However, in an Achilles tendon transection model (unsutured) we have demonstrated a small impairing effect of a systemic MMP-inhibitor on tendon healing (unpublished). This might be avoided with local treatment. The cumulative effect of local MMP-inhibitors on the total healing capacity of end-to-end sutured tendons needs further study.

By our coating method, any drug could potentially be introduced into the direct vicinity of the suture to improve suture fixation, e.g. an MMP-inhibitor, or stimulate overall healing, e.g. a growth factor, or both. The amount of drug delivered is negligible from a systemic point of view.

We imagine a broader application of this method since a similar reaction to sutures is likely to occur in any tissue, and with that, a potential to benefit from inhibition of MMPs.

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References


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