In Vitro **Degradation of Polydioxanone Lifting Threads in Hyaluronic Acid**

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Abstract

Recently, some clinicians have proposed implanting polydioxanone (PDO) threads imbibed in hyaluronic acid (HA), arguing that this may reinforce the lifting effects. However, this is controversial because PDO sutures are hydrophilic and the presence of HA could increase the rate of hydrolysis. The aim of this study was to demonstrate the degradation of PDO lifting threads in HA through ultramicroscopy. It was a qualitative research and preclinical trial. Three, 1-cm-long, segments of 23-G PDO threads were immersed in 1.5-mL non-crosslinked HA in previously labeled, sterile microcentrifuge tubes. These were observed by ultramicroscopy at $4\times$ and 10× after 24, 48, and 72 h. Microphotographs taken after 24 h show structural changes in the fibers, presenting an increase in interlaminar spaces and dilution of violet pigmentation. At 48 h, degradation continues. PDO hygroscopy is observed as aqueous content between the peripheral layers and the central core of the thread. At 72 h, as the pigment is released, larger empty spaces are observed in the central column of the thread, and there is disorganization of the peripheral fibrils with fraying all along the fiber. HA induces rapid biodegradation of the PDO thread by hydrolysis beginning 24 h after contact of the thread with the biomaterial. The non-crosslinked HA is a powerful catalyzing agent for hydrolytic degradation of the PDO thread, because this thread is highly hydrophilic. Clinically, embedding PDO threads in HA accelerates biodegradation of the suture.

Keywords: Biodegradation, hyaluronic acid, lifting threads, PDO hydrolysis, polydioxanone

Introduction

Polydioxanone (PDO) threads have been a successful therapy indicated for reverting sagging, lipomatosis, rhytidosis, and deep folds. After the threads are inserted, a fibrotic reaction takes place with the surrounding biomaterial. $[1-3]$ Thus, the lifting effect on sagging tissues is due to fibrotic paths organized during the permanence of the thread and the residual path once the suture is reabsorbed.[4] The longevity of this lifting is limited by the speed of biodegradation (hydrolysis).^[5]

In spite of important advances in Aesthetic and Regenerative Medicine, some clinicians have arbitrarily tried to popularize a clinical protocol, with no foundation in evidence-based medicine, which consists of associating PDO threads with hyaluronic acid (HA). However, we considered inadmissible this proposal because PDO is

highly hydrophilic, and thus, in the presence of HA, hydrolysis could occur very quickly. We proposed to demonstrate the degradation of PDO lifting threads in HA through ultramicroscopy.

Materials and Methods

We analyzed three segments of a monofilament of PDO brand JBP V-Lift Premium (JBP Korea), with a 23-G (4-0) diameter. Each segment of PDO thread was separately submerged in 1-mL non-crosslinked HA, INNO-TDS

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Hyaluronic Acid (no. 1567; Laboratories Innoaesthetics, Barcelona, Spain) in sterile 1.5-mL microcentrifuge tubes and incubated at 37°C. At 24, 48, and 72h after immersion, the segments were dried over a sterile field at room temperature for 15 mins, and were observed ultramicroscopically under a reflected light optical microscope (Industrial Microscope Division, Nikon Instruments, Inc. Melville, New York) at 4× and 10×.

Results

After 24h, structural changes occur in the fibers with an increase in interlaminar spaces. This is visualized more clearly in the central column of the thread where there are areas of discontinuous dilution of the violet pigment [Figure 1].

Assessment of the next segment (48h) suggests that degradation continues, observing serpentine swelling in the periphery of the thread and an increase in interlaminar spaces [Figure 2A and B].

In addition, we can visualize retention of the aqueous content between the peripheral layers and the central core of the thread (hygroscopic phenomenon), which seems to show a pattern of hydrolysis by layers or interlaminar in this second stage [Figure 2C and D].

Moreover, at 48h, there is evidence of the marked hydrolytic attack in the amorphous zones and the process continues with degradation by layers in a linear pattern [Figure 3A].

PDO suture is a thermoplastic polymer, and the vitreous transition temperature $(T_g - 16^{\circ}\text{C})^{[6]}$ is lower than the assay temperature. In this manner, as the thermic reaction moves toward the crystal, the empty spaces increase in diameter, as seen in Figure 3B.

After 72h, with the release of the pigment, we can observe empty spaces in the central column of the thread and also the disorganization of the peripheral fibrils that show up as a frayed pattern along the fiber [Figure 4A and B].

In other areas of the segment submerged for 72h, we observe the formation of small cracks, cross-wise to the suture thread, from the surface to the center (pattern of degradation heterogeneous by water is diffusing into the fiber), with a tendency to accumulate during these first hours in the peripheral zone, which possibly corresponds to the amorphous zone of the material [Figure 5A and B].

In addition, this could be related with the physical integrity of the suture during the first weeks, because it still has a central portion that has not been completely hydrolyzed. So, as the central portion or skeleton becomes more exposed to the direct action of extracellular water, the process of degradation becomes more acute, finally causing the suture to lose its stability as a fiber and leading to the excision of the smaller reported fragments, which can then be digested by the immune system.

Discussion

In PDO threads, biodegradation is caused by penetration of the fluids that break the molecules of the suture material.[7] Their rate of total loss of resistance occurs in about 63 days $[8,9]$ and the degradation occurs by excision in the amorphous regions of the material.^[10] Excision begins after 15 days and changes of the interfibrillar microstructure finally cause rupture of the thread, but in the present study, it was observed much earlier.

Thus, at 24h, changes are observed in the fiber which become more evident at 72h, as indicated by a series of empty spaces between the fibers, breakage of some peripheral fibers, and finally, loss of mass.

Figure 1: Polydioxanone (PDO) thread after 24 h of immersion in HA. (A) Reflected light microphotography of the thread at 10×, which shows the widened interlaminar and interfibrillar spaces in the central column of the thread as vertical, parallel whitish bands corresponding to the dissolution of the amorphous phase of the polymer. (B) Reflected light microphotograph of the thread at $4\times$, which shows traces of pigment being expelled toward the periphery of the thread on a central background of interlaminar and interfibrillar empty spaces corresponding to zones of fiber hydrolysis

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Figure 2: Polydioxanone (PDO) thread after 48 h of immersion in HA. (A) Microphotography of the thread at 4×. Note the central column of the thread showing a clear background surrounded by parallel layers in dark and light up to the periphery of the thread. (B) Area at $10 \times$. Note the increase in bright interfibrillar spaces seen as vertical parallel whitish bands corresponding to the dissolution of the periphery of the thread. (C and D) The thread at 4×. Retention of aqueous content is observed between the peripheral layers and the central core of the thread

Figure 3: Polydioxanone (PDO) thread after 48 h of immersion in HA. (A) Reflected light microphotography of the thread at $4 \times$. Linear pattern of the hydrolytic attack with emphasis on the central column of the thread, which is seen as an empty band. (B) Representative close-up of multiple regions of the thread that show areas of central hydrolytic degradation with possible loss of mass of the polymer

Among the most valued reasons for the use of PDO threads are their use as scaffolds for active molecules *in vivo*. [11] Despite this, associating HA with PDO tensor threads is an implausible idea from a biochemical standpoint because the non-crosslinked HA is highly hydrophilic. Moreover, the PDO suture shows poor resistance to diluted acids as $HA.$ [12]

Thus, when associating the PDO with non-crosslinked HA, the chemical resistance of the suture is further reduced. It is possible that union PDO-HA results in a third species that is responsible for the final degradation of the suture, mimicking the role of the enzyme that hydrolyzed the PDO.[12]

Conclusion

The non-crosslinked HA is a powerful catalyst for the hydrolytic degradation of the PDO thread because the latter is highly hydrophilic and induces the rapid biodegradation of the PDO thread, which begins after 24h of contact of the thread with the biomaterial. We propose that, clinically, administrating HA could be indicated when facing complications for superficial placement of support threads, fulfilling the purpose of accelerating biodegradation of the thread in the patient.

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Figure 4: Polydioxanone (PDO) thread after 72 h of immersion in HA. (A and B) Optical microphotography of the thread at 4× showing a frayed pattern on the periphery of the thread

Figure 5: Polydioxanone (PDO) thread after 72 h of immersion in HA. (A and B) Optical microphotography of the thread at 10×. Arrows show transversal cracks due to migration of the amorphous zone to the crystalline zone of the polymer in the suture

Conflicts of interest

There are no conflicts of interest.

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