

# Usefulness of polydeoxyribonucleotide as an alternative to corticosteroids in patients with lateral epicondylitis

## A case series

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### Abstract

**Rationale:** Local corticosteroid injections are commonly used as an easy, cost-effective treatment for patients with lateral epicondylitis (LE). Despite their strong anti-inflammatory effect, repeated injections of corticosteroids are not recommended in LE because they can aggravate tearing of the tendons.

**Patient concerns:** A 65-year-old (Case1) man and a 59-year-old (Case2) man had a 2-month history of right lateral elbow pain exacerbation.

**Diagnoses:** Lateral epicondylitis with hypervascularity of the common extensor tendon.

**Intervention:** After informed consent was provided, ultrasound (US)-guided polydeoxyribonucleotide (PDRN) injections were made into on the common extensor tendons of both patients.

**Outcomes:** After 2 weeks from PDRN injection, both patients reported significant pain relief. The US 2 weeks after the PDRN injection showed that the hypervascularity of the common extensor tendon in both patients had been completely cured, although there was no significant change in the findings of tendinosis.

**Lessons:** PDRN may be useful for patients with LE because there were no negative effects on tendon cells and tissues in previous in vitro and in vivo studies, despite its anti-inflammatory effects.

**Abbreviations:** LE = lateral epicondylitis, NRS = numerical rating scale, PDRN = polydeoxyribonucleotide, US = ultrasound.

**Keywords:** lateral epicondylitis, polydeoxyribonucleotide, tennis elbow, ultrasound

## 1. Introduction

Lateral epicondylitis (LE) is the most common cause of elbow pain in adults, and it can be defined as an overuse injury occurring on the lateral side of the elbow where the common extensors originate from the lateral epicondyle.<sup>[1]</sup> Despite the high incidence of LE, optimal treatment it has not been established, and numerous treatment options, including therapeutic exercise, bracing, corticosteroid injection, shock wave or ultrasound therapy, and surgical decompression have been used to treat

LE.<sup>[2]</sup> Of these treatment choices, local corticosteroid injections are commonly used as an easy, cost-effective treatment for patients with LE.<sup>[2,3]</sup> Despite its strong anti-inflammatory effect, repeated injections of corticosteroids are not recommended in LE because they can aggravate tearing of the tendons.<sup>[3]</sup> In in vitro experiments, the local administration of corticosteroids has significant negative effects on tendon cells, including reduced cell viability, cell proliferation, and collagen synthesis.<sup>[4]</sup> In in vivo studies, there is also increased collagen disorganization and necrosis, and the mechanical properties of the tendons are also significantly reduced.<sup>[5]</sup>

Recently, several studies have found that polydeoxyribonucleotide (PDRN) can be a substitute for corticosteroids because it has anti-inflammatory capabilities with a fewer side effects.<sup>[6–8]</sup> PDRN is formed by deoxyribonucleotide polymers with chain lengths ranging between 50 and 2000 base pairs, and is known to have an anti-inflammatory effect similar to corticosteroids.<sup>[6]</sup> However, unlike corticosteroids, it has been reported that PDRN improves tendon healing in a mouse model of tendon rupture.<sup>[9]</sup> Despite this, there have been no reports on its effectiveness in patients with LE yet. Here, we report 2 cases of improved LE after local administration of PDRN. This case series was approved by ethics committee of our hospital.

## 2. Methods

In this case series, we retrospectively reviewed all patients who had received PDRN from among LE patients who visited Daegu Fatima Hospital from January 1, 2016 to February 28, 2018.

Editor: N/A.

This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Science, ICT and Future Planning (NRF- 2017R1D1A1B03033127).

The authors declare no conflict of interests.

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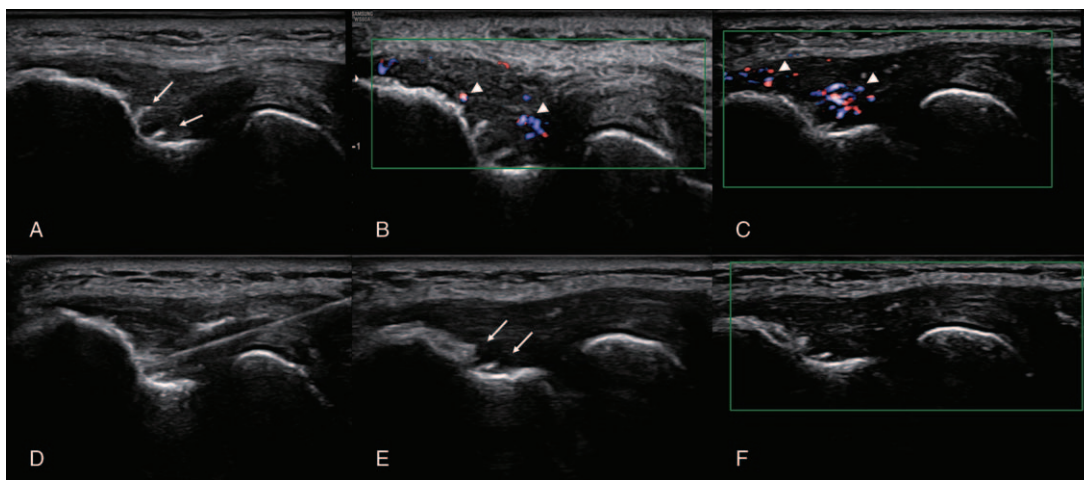
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Medicine (2018) 97:20(e10809)

Received: 29 January 2018 / Accepted: 25 April 2018

<http://dx.doi.org/10.1097/MD.00000000000010809>



**Figure 1.** Lateral epicondylitis in a 65-year-old man with tendinosis of the right common extensor tendon. A–C, Longitudinal US image of the common extensor tendon origin shows hypervascularity (arrow heads), marked heterogeneity with numerous hyperechoic calcifications (arrows) and hypoechoic intrasubstance tears throughout the tendon, findings consistent with severe chronic tendinosis. D, Local administration of polydeoxyribonucleotide (PDRN) was performed on the common extensor tendon. E & F, Ultrasound imaging of the common extensor tendons obtained two weeks after the procedure showed complete resolution of hypervascularity, although there was no significant change in the findings of tendinosis.

Data were collected from patients' medical records including demographics, medication history, past medical history, clinical evaluation, and ultrasound imaging. The study was approved by the Institutional Review Board of Daegu Fatima Hospital, and all patients in this case series have provided informed consent for publication.

### 3. Results

#### 3.1. Case 1

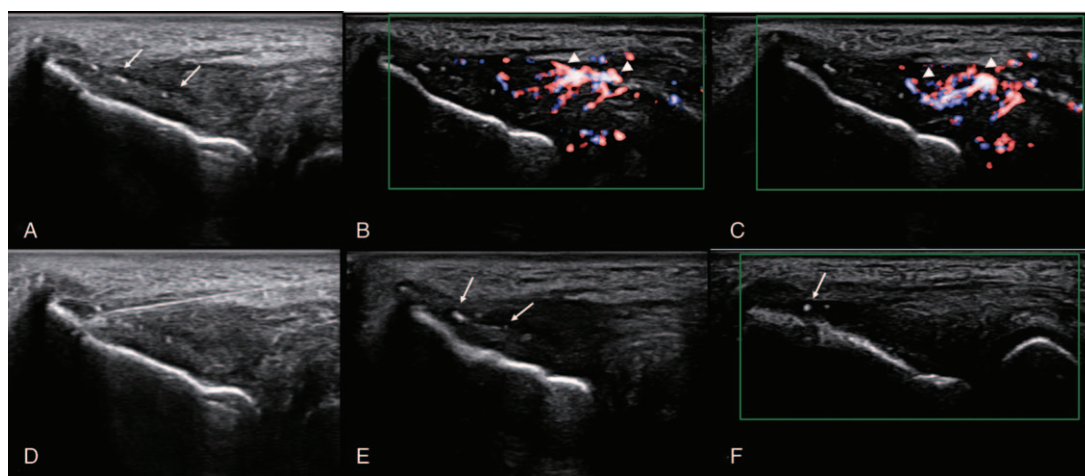
A 65-year-old man reported a 2-month history of right elbow pain exacerbation. He visited the outpatient clinic for right elbow pain that worsened when he clenched a fist or held something in his hand. He was a farmer, and did not partake in any recreational sports. From his physical examination, Cozen's test on the right elbow pain was positive for pain, and the pain was described as sharp and achy, with an intensity of 7/10 on the numerical rating scale (NRS).<sup>[10]</sup> There was also tenderness at the origin of the right common extensor tendon. However, he did not complain of any weakness of grip strength.

Ultrasound (US) evaluation of the right shoulder was performed in the outpatient clinic with an Accuvix V20 ultrasound system and a 5- to 13-Hz broadband linear transducer (Samsung Medison, Hongchun, Korea). From the US, marked heterogeneity with numerous hyperechoic calcifications and hypoechoic intrasubstance tears throughout the tendon, findings consistent with severe chronic tendinosis (Fig. 1A), and hypervascularity (Fig. 1B, C) were shown in the common extensor tendon origin. He was well informed about the treatment of LE and agreed to use PDRN because he was worried about the side effects of corticosteroids. After informed consent was given, the patient then underwent US-guided PDRN injection into the common extensor tendons using 5.625 mg/3 mL of PDRN (Rejuvenex, PharmaResearch Products, South Korea), with a 27 gauge, 1.5 inch needle (Fig. 1D). After the injection, he was educated on posture; he was advised to avoid excessive clenching of his fist and extending his wrist if possible. Two weeks after the PDRN injection, he reported significant pain relief, with a decrease of NRS from 7 to 1. Although there was no significant change in the findings of tendinosis in a follow-up US 2

weeks after the PDRN injection (Fig. 1E), US imaging of the common extensor tendons showed complete resolution of hypervascularity (Fig. 1F). At the 2-month follow-up, he demonstrated an improvement in the LE symptoms without any complications. He reported that he was not inconvenienced in daily life, although he had mild pain when he clenched his fist strongly or lifted a heavy object.

#### 3.2. Case 2

A 59-year-old man reported a 2-month history of right elbow pain exacerbation. He visited the outpatient clinic for right elbow pain that worsened when he clenched a fist or held something in his hand. He enjoyed no other sports activities beside golf. He had played golf once a week for 7 years. From his physical examination, Cozen's test on the right elbow pain was positive for pain, and the pain was described as sharp and achy, with an intensity of 7/10 on the NRS. There was also tenderness at the origin of the right common extensor tendon, and he complained of mild weakness of grip strength. From the US, marked heterogeneity with numerous hyperechoic calcifications and hypoechoic intrasubstance tears throughout the tendon, findings consistent with severe chronic tendinosis (Fig. 2A), and hypervascularity (Fig. 2B, C) were shown in the common extensor tendon origin. After informed consent was given, the patient then underwent US-guided PDRN injection into the common extensor tendons using 5.625 mg/3 mL of PDRN (Rejuvenex, PharmaResearch Products, South Korea), with a 27 gauge, 1.5 inch needle (Fig. 2D). After the injection, he was educated on posture; he was advised to avoid excessive clenching of his fist and extending his wrist if possible. Two weeks after the PDRN injection and education about posture, he reported significant pain relief, with a decrease in NRS from 7 to 2. The US 2 weeks after PDRN injection showed there was no significant change in the findings of tendinosis (Fig. 2E), but the hypervascularity of the common extensor tendon was completely resolved (Fig. 2F). At the 2-month follow-up, he demonstrated an improvement in the LE symptoms without any complications. He reported that he was not inconvenienced in daily life, although he had mild pain when he clenched his fist strongly or lifted a heavy object.



**Figure 2.** Lateral epicondylitis in a 59-year-old man with tendinosis of the right common extensor tendon. A–C, Longitudinal US image of the common extensor tendon origin shows hypervascularity (arrow heads), marked heterogeneity with numerous hyperechoic calcifications (arrows) and hypoechoic intrasubstance tears throughout the tendon, findings consistent with severe chronic tendinosis. D, Local administration of polydeoxyribonucleotide (PDRN) was performed on the common extensor tendon. E & F, Ultrasound imaging of the common extensor tendons obtained two weeks after the procedure showed complete resolution of hypervascularity, although there was no significant change in the findings of tendinosis.

#### 4. Discussion

PDRN is obtained from trout or salmon sperm through an extraction process that entails high temperature sterilization and purification to obtain a >95% pure, active compound without any other pharmacologically active peptides or proteins. PDRN is known to stimulate A2A receptors.<sup>[11]</sup> Adenosine, a purine nucleoside that is released from a variety of cells in response to several types of stress, has been suggested to regulate inflammation via an interaction with one or more of its four known receptors (A1, A2A, A2B, and A3).<sup>[11]</sup> Although adenosine receptor stimulation has differing effects on the release of pro-inflammatory cytokines, adenosine A2A receptor stimulation specifically has been shown to inhibit TNF- $\alpha$  production in human peripheral blood mononuclear cells.<sup>[11]</sup> Moreover, PDRN has revealed that it can markedly potentiate anti-inflammatory IL-10 production and induce a significant decrease in pro-inflammatory IL-12 and TNF- $\alpha$  secretion without cytotoxicity in macrophages stimulated by lipopolysaccharide, an inflammation inducer.

In the cases reported in this paper, both patients with LE received US-guided PDRN injections into the common extensor tendon, and showed improvements in their symptoms. This effect is thought to be due to the anti-inflammatory effect of PDRN, which reduces pro-inflammatory cytokines such as IL-1 and 6, and increases anti-inflammatory cytokines such as IL-10, as demonstrated in previous studies.<sup>[9,11]</sup> In patients with LE, repeated injections of corticosteroids can aggravate tearing of the tendons. However, PDRN can be useful for patients with LE because there were no negative effects on tendon cells and tissues in previous *in vitro* and *in vivo* studies, despite its anti-inflammatory effects.

#### 5. Conclusion

This is the first report on the LE of PDRN, and although several studies have reported its effectiveness via other routes of

administration, we suggest that additional studies on the safety and long-term effect of PDRN in LE are necessary.

#### Author contributions

**Conceptualization:** Goo J. Lee.

**Writing – original draft:** Donghwi Park.

**Writing – review & editing:** Donghwi Park.

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