Implantation of an Acellular, Bioresorbable, Ultra-Purified Alginate Gel after Discectomy for Lumbar Intervertebral Disc Herniation: An Interim Analysis of a First-In-Human Pilot Study

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INTRODUCTION:

Herniated nucleus pulposus (NP), one of the most common diseases of the spine, is surgically treated by removing the sequestered NP. However, intervertebral disc (IVD) defects may remain after discectomy, which leads to inadequate tissue healing and predisposes patients to IVD degeneration. An acellular, bioresorbable, ultra-purified alginate (UPAL) gel implantation system can be used to fill any IVD defects to prevent IVD degeneration after discectomy (Figure 1). This first-in-human pilot study aimed to determine the feasibility, safety, and perceived patient response to a combined treatment with discectomy and UPAL gel implantation for herniated NP.

METHODS:

We designed a single-arm, double-center, open-label pilot trial. The study started in November 2018 and recruitment of patients ended in September 2020. Patients aged 20–49 years, diagnosed as having isolated lumbar IVD herniation, and scheduled for discectomy represented the suitable candidates. All eligible participants who provided informed consent underwent standard discectomy, followed by UPAL gel implantation (Figure 1). The primary outcomes of the trial were the feasibility and safety of the procedure. The secondary outcomes included self-assessed clinical scores for evaluating pain and health-related quality of life, and magnetic resonance imaging (MRI)-based measures of morphological and compositional qualities of the IVD tissue. The initial outcomes were published at 24 weeks, with prospective follow up at 96 weeks (2 year) postoperatively. Feasibility and safety analyses were performed using descriptive statistics. Intention-to-treat and per-protocol analyses of the treatment effectiveness trends were conducted.

RESULTS:

Forty patients (30 men and 10 women; mean age: 36.3 y) were enrolled in the study and all patients completed the initial 6-month postoperative follow up. The IVD herniation levels were L4/L5 in 10 patients and L5/S in 30 patients. All patients underwent discectomy and underwent UPAL gel implantation. Regarding the primary outcome, the feasibility of UPAL gel implantation was 100%. No adverse events occurred after UPAL gel implantation, and the safety of the procedure was 100%. Within 6 months after surgery, 2 of the 40 patients (5%) had recurrent herniation, requiring reoperation. Of the 38 cases excluding 2 cases with recurrences of herniation, 28 were followed up for 2 years after surgery.

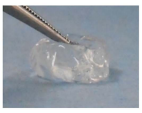
The secondary outcome of pain assessment showed that the visual analog scale (VAS; 0-100 mm, with higher scores representing worse pain) scores for low back and lower extremity pains improved significantly from 1 to 96 weeks postoperatively as compared with the preoperative scores (Figure 2). The Japanese Orthopaedic Association (JOA) score, Oswestry Disability Index (ODI), and VAS score improved significantly after surgery (Figure 2). MRI analysis showed that the Pfirrmann disc degeneration grade improved significantly at 24 weeks postoperatively compared to preoperatively and was maintained until 96 weeks postoperatively (Figure 3). In quantitative MRI analysis for IVD, diffusion-weighted imaging (DWI) showed that normalized apparent diffusion coefficient values of lesioned IVD was significantly lower at 24 weeks postoperatively than preoperatively, and was comparable to preoperative values at 96 weeks postoperatively. T1rho and T2star imaging revealed equivalent normalized T1rho and T2star values of lesioned IVD between the preoperative, 24-wwk and 96-week postoperative states. (Figure 3)

DISCUSSION AND CONCLUSION:

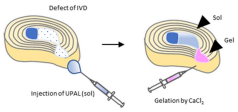
This first-in-human pilot study confirmed the feasibility and safety of UPAL gel implantation for herniated NP after discectomy. The secondary outcomes and clinical scores for evaluating pain and health-related quality of life improved significantly from the immediate to the 96-week postoperative period as compared with the preoperative period.

In terms of pain score, the postoperative VAS scores for low back and lower extremity pains in this study tended to be lower than those in previous reports of herniated disc surgery. However, the fundamental clinical results and findings from the MRI analysis of lumbar discectomy have not been reported. Therefore, a historical controlled trial of herniated discectomy without UPAL gel implantation using the same evaluation methods and protocols as in the present clinical study is underway as a comparative control study. In addition, we plan to conduct a pivotal randomized controlled trial based on these results.

Figure 1. Bioresorbable ultra-purified alginate (UPAL) gel



UPAL gel



UPAL gel implantation after discectomy

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Figure 2. Clinical scores before and after UPAL gel implantation

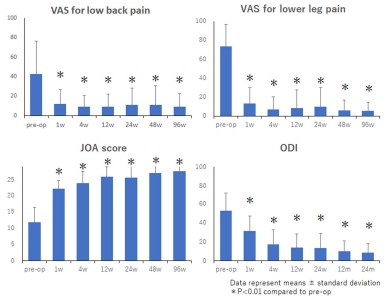

Figure 3. MRI analysis before and after UPAL gel implantation