Efficacy of Submucosal Polydeoxyribonucleotide Injection After Impacted Mandibular Third Molar Extraction: A Randomized Controlled Trial

Hyun Joong Kim

Department of Medicine
Graduate School
Yonsei University

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Hyun Joong Kim

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This Certifies that the Master's Thesis of Hyun Joong Kim is Approved

Committee Chair	**Chunui Lee**
Committee Member	**Pil Young Jung**
Committee Member	**Chun Sung Byun**

Department of Medicine
Graduate School
Yonsei University
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ABSTRACT

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Purpose: This study aimed to evaluate the efficacy of polydeoxyribonucleotide (PDRN) injection after impacted mandibular third molar extraction. The primary outcome was postoperative pain, while secondary outcomes included postoperative swelling, periodontal pocket depth, and patient-reported outcome.

Materials and Methods: Thirty medically uncompromised patients who underwent bilateral extraction of impacted mandibular third molars were enrolled in the clinical study. PDRN was randomly injected on the experimental side, while normal saline was injected on the control side. Postoperative pain was assessed using a visual analog scale (VAS). Postoperative swelling was evaluated via linear measurements based on the Laskin method. Furthermore, three-dimensional volumetric analysis was conducted by superimposing serial facial scans obtained at baseline (preoperatively), and on postoperative days 3 and 7. Pocket probing depth was evaluated using a periodontal probe. Patient's postoperative morbidity and subjective perceptions were evaluated using the patient-centered outcome questionnaire (PCOQ). Statistical software was used to evaluate the data, p-value<0.05 was considered statistically significant.

Results: Patients demonstrated statistically verifiable reductions in postoperative pain, swelling, and discomfort on the experimental side.

Conclusion: The results suggest that PDRN injection can be a suitable option to mitigate postoperative complications after impacted mandibular third molar extraction. However, further randomized controlled trials are required to confirm the reliability of the study and verify its suitability.

Keywords: Oral Surgery; Polydeoxyribonucleotides; Postoperative Complications; Computer-Assisted Image Processing; RCT design

1. Introduction

Impacted mandibular third molar (IMTM) extraction is one of the most commonly performed surgical procedures in oral surgery.[1)] IMTMs are frequently associated with various pathological conditions including pericoronitis, dental caries, odontogenic tumors, neurogenic pain, and periodontal defects adjacent to the second molar.[2),18),30)] IMTM extraction typically necessitates mucoperiosteal flap elevation and osteotomy, which inevitably lead to soft tissue damage and alveolar bone resorption.[3)] Postoperative pain and swelling should be optimally managed and reduced to improve the patient's quality of life (QOL). The recovery of periodontal tissues after IMTM surgery should also be considered. Accordingly, efforts are ongoing to identify therapeutic molecules that can alleviate postoperative inflammatory complications through local or systemic administration following IMTM surgery.[4),13)]

Polydeoxyribonucleotides (PDRN), derived from the sperm of *Oncorhynchus mykiss* or *Oncorhynchus keta* are low molecular weight DNA fragments known for their ability to 1) stimulate cell migration and growth, 2) promote extracellular matrix (ECM) protein production, 3) reduce inflammation by suppressing pro-inflammatory cytokine secretion and 4) enhance wound healing.[5),6),7)] Their beneficial effects such as promoting cell migration, growth, and angiogenesis while attenuating inflammation have been demonstrated in skin regeneration in both preclinical and clinical studies (1990-2016).[8)] As a regenerative agent, PDRN has been widely used in various medical fields, including diabetic foot ulcers, thermal injuries, rheumatoid arthritis, and skin cosmetics.[9).10)] However, the clinical application of PDRN in dentistry especially in the oral surgery field remains relatively unknown.[10)] Therefore, this clinical study is the first to evaluate the effect of submucosal PDRN injection (PI) after IMTM extraction. A prospective, randomized, split-mouth clinical trial was conducted in 30 medically uncompromised patients who had undergone bilateral extraction of IMTMs by a single surgeon.[2),4)] As an experimental group, PDRN was injected randomly on one side. As a control group, normal saline was injected on the opposite side. Postoperative pain was measured as a primary outcome, to dictate sample size

requirements and statistical power. Postoperative swelling, pocket probing depth, and patient-centered outcome questionnaire (PCOQ) were measured as secondary outcomes to evaluate the effect of submucosal PI.

2. Materials and Methods

2.1. Study design and patients

An initial pilot study was conducted with five patients (10 IMTMs) to estimate the sample size for the clinical trial. Based on this pilot data, the null hypothesis was statistically rejected with a statistical power of 80% and significance level of 0.05.[11] Based on the mean visual analog scale (VAS) scores of the pilot study (PDRN 0.80 ± 0.84 and placebo 1.80 ± 1.92), a sample size of 30 patients was estimated.[2),12)] To evaluate the effect of PI on postoperative variables, a prospective randomized, double blinded study was conducted from September 2024 to February 2025.[1),2)] Thirty patients who did not have any medical problems that could influence the surgical procedure and postoperative wound healing were enrolled in the clinical study as shown in **Table 1)**.[2)] In a split-mouth design involving 30 patients and 60 surgical sites, PDRN was administered to 16 left-sided and 14 right-sided sites, with normal saline injected contralaterally as a control. Patients with bilateral IMTMs of comparable surgical difficulty, as evaluated according to the Winter, Pell and Gregory classification, and with well-controlled systemic conditions were included. Exclusion criteria comprised autoimmune diseases, hemorrhagic disorders, and psychiatric disorders or suspected psychiatric conditions. Participants were also excluded based on the presence of known hypersensitivity to polydeoxyribonucleotide (PDRN), pregnancy, a confirmed diagnosis of malignancy or ongoing chemotherapy, and a history of alcohol dependence. Additionally, any individual considered unsuitable for study participation based on the investigator's discretion was excluded.[4),15)] The Institutional Review Board (IRB) of *** approved the study (IRB No. ***). This study has been registered with the Clinical Research Information Service (CRIS) of the Korea Disease Control and Prevention Agency (CRIS No. KCT0010231). All patients were referred to the Department of Oral and Maxillofacial Surgery and were recommended for bilateral extraction of IMTMs. Written informed

consent was obtained from all patients, who voluntarily agreed to undergo the procedure and declared their willingness to return at regular intervals for evaluation at 3, 7, 14, and 60 days after surgery.[13),14),15)]

2.2. Blinding

Information regarding the type of injection administered at each extraction site was concealed from the patient, operator, evaluator (responsible for examinations and outcome measurements), and statistician. An external study collaborator, independent of the operator and evaluator, was responsible for allocating participants to the experimental and control groups and assigning the random sequence to ensure allocation concealment. Prior to the surgical intervention, a sealed envelope containing a randomized list of PDRN injection sites was securely held by the external study collaborator, who had no further involvement in the clinical trial. The assigned interventions were prepared in identical syringes with the same packaging and appearance to maintain blinding. Data recording and statistical analysis were conducted using group codes ‘A’ for PDRN and ‘B’ for placebo, using Microsoft Excel (Microsoft, Redmond, WA, USA). The randomization code was not disclosed until completion of all clinical procedures and statistical analyses.[11)]

2.3. Surgical procedures and further management

All surgeries were performed by a single surgeon (K.H.J) on the same day under local anesthesia. All patients were radiologically screened with a panoramic X-ray and cone-beam computed tomography (CS 9600, Carestream Dental LLC. 3625 Cumberland Blvd. Ste. 700 Atlanta, GA 30339 USA) to assess the anatomical relationship between the inferior alveolar nerve and both IMTMs.[16,)17),18)] All surgeries were performed under strict aseptic conditions to prevent cross-contamination. Patients were informed that they would receive a PDRN

injection on one side but were not informed of which side was allocated to PDRN. Consecutive IMTM surgeries were performed in order of random assignments.[2] All patients rinsed their mouths for 1 min with a 0.2% Chlorhexidine mouthwash before surgery. Bilateral inferior alveolar nerve block anesthesia and infiltration anesthesia (lidocaine HCl 2% injection Daihan, Daihan PharmCo. Ltd, Seoul, Korea) were given on both surgical sites. Vertical and horizontal incisions were made on the buccal side of the mandibular second molar to carefully elevate the mucoperiosteal flap. Osteotomy was done using a carbide fissure bur (SSW HP-702, SS White Dental, 1145 Towbin Ave, Lakewood, NJ USA) and low-speed straight hand-piece (NSK EX-6, Nakanish inc. 700 Shimohinata, Kanuma, Tochigi 322-0075 Japan) 200,000 rpm under sufficient saline irrigation. To ensure that a surgeon remained blinded to the allocation of the experimental and control sides, an external study collaborator prepared and provided the assigned injections. Polydeoxyribonucleotide (PDRN, Zerone Cellvane Korea, 542 Eonju-ro, Gangnam-gu Seoul Korea) injection was done on the experimental side. A total of 1.0 mL (1.875mg of PDRN) was injected in the base of a mucoperiosteal flap, 0.5 mL in the mesial margin, and 0.5 mL in the distal margin.[4),15)] On the control side, a saline solution of 1.0 mL was administered as a placebo in the same manner. After the extraction of IMTMs, the elevated mucoperiosteal flap was repositioned, and simple interrupted sutures were applied. Every patient received oral medication including antibiotics (cefditoren pivoxil 100 mg thrice daily), and an analgesic (aceclofenac 100 mg thrice daily) for five days after IMTM surgery. **Fig.1,2)** Patients were monitored throughout the follow-up period for clinical signs of inflammation, including erythema, swelling, pain, discoloration, and functional impairment. When systemic inflammation was suspected, C-reactive protein (CRP) and interleukin-6 (IL-6) were evaluated. Fortunately, no instance of systemic inflammation was identified in any of the cases.[19)] To minimize the risk of cross-contamination, patients were instructed to maintain good oral hygiene throughout the clinical trial period. At each follow-up visit, atraumatic bilateral intraoral dressing was performed without disrupting the healing process while maintaining the integrity of the blood clot.

2.4. Postoperative examinations

Patients were selected according to the inclusion criteria, underwent general physical examination, filled out information sheets, signed the informed consent for PI, and took the random number. To minimize the risk of bias resulting from maintaining blinding of the study, a surgeon who had not operated on patients conducted postoperative examinations, collected questionnaires and reported all postoperative information to avoid any underestimation of the complications. The primary outcome of the study was postoperative pain. The occurrence of postoperative swelling, changes in pocket probing depth to assess periodontal tissue recovery 2 months after surgery, and PCOQ evaluating postoperative quality of life were adopted as secondary outcome measures in the present study. Postoperative pain and swelling were measured at postoperative day 3 (POD3); as this marks the peak of acute inflammatory response.[20),21)] Postoperative pain and swelling were measured on POD7; since the blood clot was progressively replaced by granulation tissue and inflammatory responses began to subside. POD 14; as granulation tissue undergoes further maturation and woven bone formation begins, pain duration time and PCOQ were assessed.[21)] Finally, pocket probing depth was measured for long-term follow-up (POD 60).

1) Pain

Pain during postoperative periods (POD3 and POD7) was evaluated using a VAS of 10 units in combination with a graphic rating scale ranging from 0 (absence of pain or discomfort) to 10 (maximum pain or discomfort).[2),22)] At 14 days after surgery, patients were questioned as to how many days their pain had persisted.

2) Postoperative swelling

Facial swelling was assessed using a tape measure and quantified as the sum of two linear measurements along defined reference points. The reference points

included the tragus (T), oral commissure (O), lateral canthus of the eye (L), and gonion (G). The horizontal measure corresponded to the distance between the T, and O. The vertical measure corresponded to the distance between the L and G.[23] **Fig.3)**

The arithmetic sums of the two measurements determined the facial measurements. The percentage of facial swelling was obtained from the difference between measurements made in the preoperative and postoperative periods, dividing the result by the value obtained in the preoperative period, and multiplying it by 100. The amount of change of linear measurement from preOP to POD3 (ΔPOD3−preOP) and from preOP to POD7 (ΔPOD7-preOP) were calculated as the amount of facial swelling and compared between the control and experimental sides.[1),23)]

Preoperatively, all patients underwent 3d facial scanning using CS Face Scan Kit (CS 9600, Carestream Dental LLC. 3625 Cumberland Blvd. Ste. 700 Atlanta, GA 30339 USA). The CS Face Scan function is launched via CS Imaging 8 software to scan and reproduce the face of a subject with a 3-dimensional render in less than 15s.[24),25)]

The study involved three time points; **Fig 4)**
- PO: face scan before surgery, point 0 **Fig 4A)**
- P3: 3 days after surgery, point 3 **Fig 4B)**
- P7: 7 days after surgery, point 7 **Fig 4C)**

At POD3 and POD7 after surgery, the second and third 3D facial scan (P3, P7) were performed to assess postoperative swelling.[24)]

Scans were exported in STL files and imported within a dental application software Materialise MIMICS 21.0 software (Materialise HQ Technologielaan 15 3001 Leuven. Belgium). Materialise Mimics software allows the user to evaluate physical models from digital facial scans. Superimposition of preoperative and postoperative scans was performed to quantify the amount of volumetric difference

between the two groups.[24] The STL files were imported into the software Materialise 3-matic version 18.0 for superimposition of the pair of scans (P0-P3 and P0-P7) using the "part comparison" specific tool. The analysis function was used to quantify the measurement of postoperative swelling by visualizing the volumetric difference between the pair of scans via a histogram through a color map.[25),26),27),28)] **Fig 5)**

3) Periodontal probing depth

Since almost all granulation tissue is replaced by woven bone between 6–8 weeks post-extraction[20).21)], periodontal probing depth (PPD) measurements were performed for long-term follow-up to evaluate the healing of periodontal tissues and to assess epithelial regeneration.[21)] Right after surgery and at 2 months after surgery, probing depths on the buccal, distal, lingual, and mesial surfaces of the adjacent second molar were evaluated. To minimize the risk of bias resulting from maintaining blindness in the study, all measurements were recorded to the nearest millimeter by the evaluator who had not operated on the patients. A periodontal probe (PDT Sensor Probes. Zila, Fort Collins. CO) was used for evaluation. PPD reduction defined as change (mm) in PPD was evaluated from baseline (the day of the surgery) to 2 months follow-up recall.[28).29)]

4) Patient-centered outcome questionnaire

To evaluate patient`s quality of life after surgery, patients filled out the PCOQ at POD 14. Patients were asked to answer a set of 11 questions, right and left sides, which were based on the Oral Health Impact Profile (OHIP) by Slade and Spencer.[4),30)]

2.5. Statistical analysis

The normality of the data was assessed using the Shapiro–Wilk test, and all variables were found to follow a normal distribution ($p > 0.05$). Accordingly, a

parametric test, the paired Student's t-test, was employed to compare outcomes between the PDRN and placebo groups in accordance with the split-mouth study design. Statistical significance was evaluated for differences in measurement values of pain duration time, postoperative pain, swelling, periodontal probing depth, and PCOQ. (p-value < 0.05) Continuous variables are presented as means ± standard deviations. As postoperative pain (VAS) and facial swelling (%) were measured at two time points (POD3 and POD7), Bonferroni correction was applied to adjust for multiple comparisons, thereby reducing the risk of type I error due to repeated measurements and ensuring more stringent control over false-positive findings. All data acquisition and analyses were performed with Microsoft Excel (Microsoft, Redmond, WA, USA) and IBM SPSS Statistics software for Windows (ver. 22.0; IBM Corp., Armonk, NY, USA).

Variable	Total
Race/Ethnicity	n(%)
Asian (East Asian)	27(90%)
Asian (Southeast Asian)	2(6.7%)
Caucasian	1(3.3%)
Sex	n(%)
Male	23(76.7%)
Female	7(23.3%)
Age (mean ± SD)	28.87±12.07

Table 1. Demographic characteristics

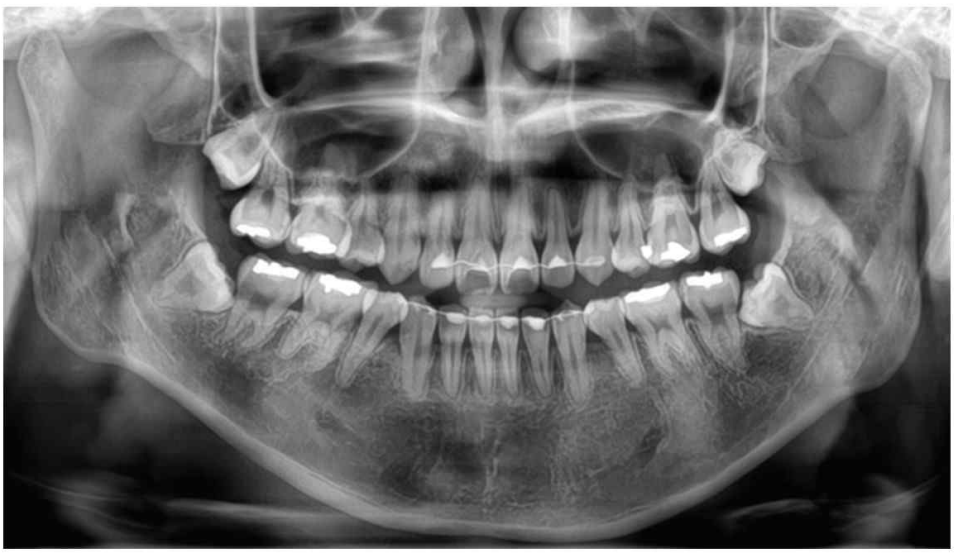


Figure 1. Preoperative panoramic X-ray

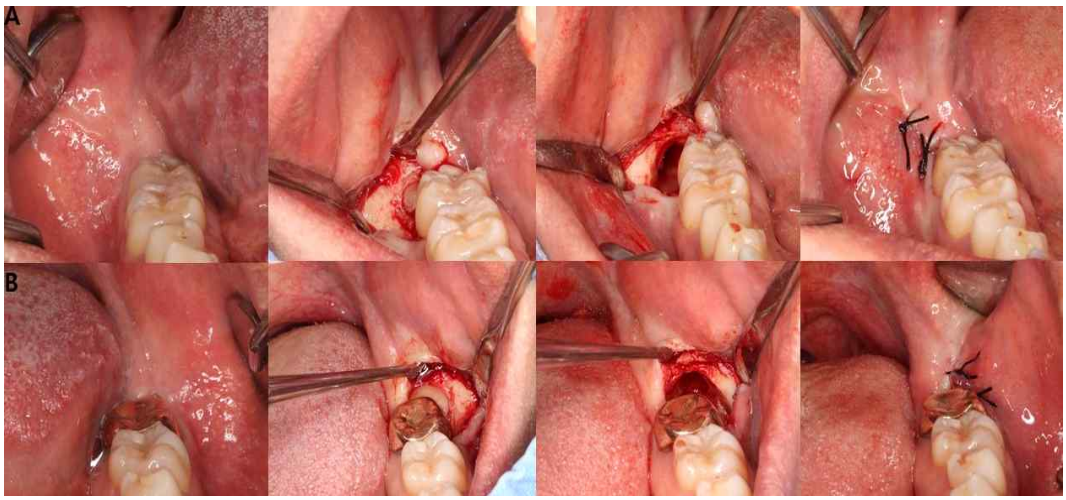


Figure 2. Intra-operative Photos
A.Experimental group (PDRN)
B.Control group (Normal Saline)

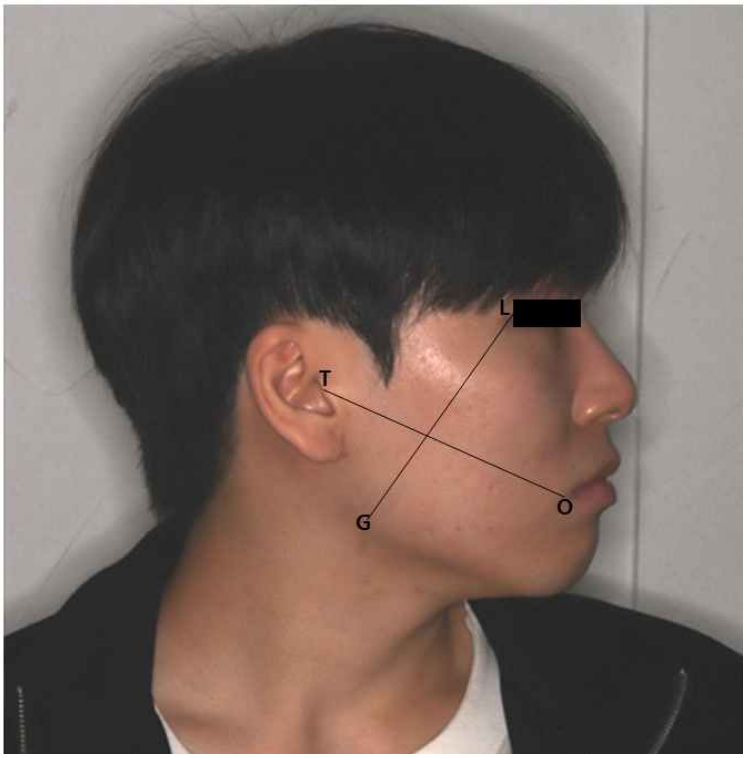
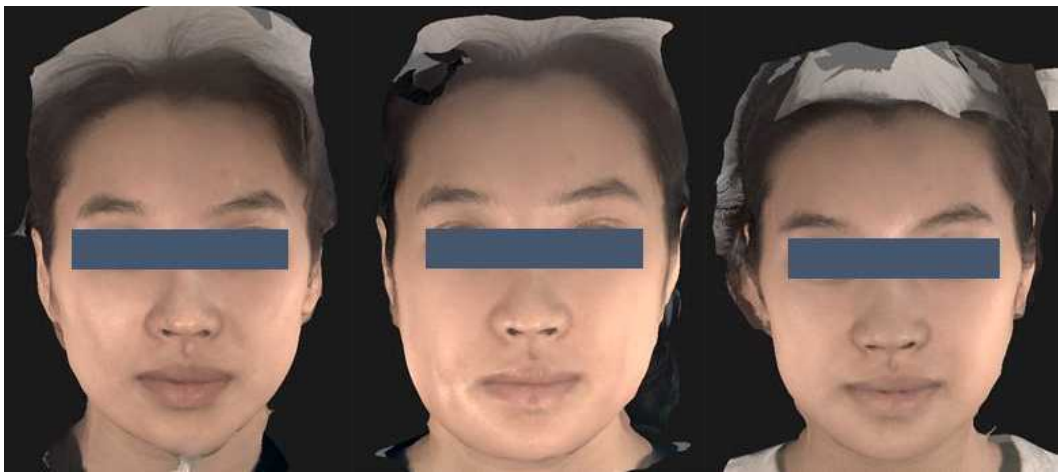


Figure 3. Reference points in linear measurement for facial swelling
A.Tragus(T)-Oral Commissure(O)
B.Lateral Canthus(L)-Gonion(G)
Facial swelling was calculated as a sum of two linear measurements



(A) (B) (C)

Figure 4.A.Preoperative scan
B.Postoperative scan (POD 3)
C.Postoperative scan (POD 7)

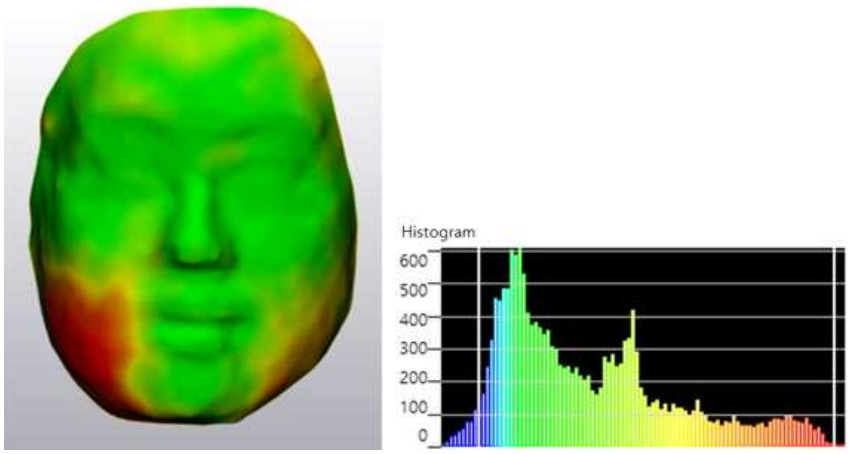


Figure 5. Qualitative analysis of the facial swelling scans at different time point
Red color represents an increase in facial swelling while blue indicates reduction. In the comparison between P0-P3, greater degree of swelling is observed on the right side(placebo) while a relatively small amount of edema is shown on left side(PDRN) as shown in the color map.

3. Results

The comparative analysis of clinical outcomes between the experimental(PDRN) and control(placebo) groups is presented in **Table 2).** Each clinical parameter was assessed to evaluate the therapeutic efficacy of PDRN, incorporating both objective clinical indicators and patient-reported outcome measures. A detailed explanation of the findings for each variable is provided in the sections below.

1) Pain

The mean pain duration of the experimental and control groups were 3.16±2.26 and 4.16±3.16. There was no statistical difference in the baseline value of pain duration between the experimental and control groups (*p*-value 0.082).

The mean postoperative pain scores of the experimental and control groups were 3.13±1.92, 4.25±1.94 at POD3, and 0.43±0.85,1.36±1.81 at POD7, respectively. After Bonferroni correction for two time-point comparisons (POD3 and POD7), the experimental group showed marked reduction of pain scores than the control (adjusted *p*-values = 0.027, 0.012).

2) Postoperative swelling

The mean percentage of facial swelling of the experimental and control groups were 3.24±2.22, 5.39±2.56 at POD3 and 0.27±0.71, 1.29±1.97 at POD7. Following Bonferroni correction for two time-point comparisons (POD3 and POD7), a statistically verifiable reduction in postoperative swelling was observed in the experimental group (adjusted *p*-values = 0.002, 0.012). As seen in the following clinical image, a marked difference between the experimental and control sides can be observed.[3] **Figure 6)**

3) Periodontal probing depth

At 2 months after surgery, the mean probing depth was 3.12±1.16 in the experimental group and 3.25±1.22 in the control group. There was no statistical

difference between the experimental and control groups regarding the PPD. (*p*-value 0.164)

4) Patient-centered outcome questionnaire(PCOQ)

The total sum mean of all patient's PCOQ scores was measured as 18.7±6.89 in the experimental group and 24.3±6.18 in the control group. Patients showed on improvement in QOL in the experimental group compared to the control group in terms of PCOQ (*p*-value 0.010)

POD	PDRN	Placebo	P-value
Pain Duration Time (Day)			
14	3.16±2.26	4.16±3.16	0.082
VAS score			
3	3.13±1.92	4.25±1.94	0.027
7	0.43±0.85	1.36±1.81	0.012
Facial swelling (%)			
3	3.24±2.22	5.39±2.56	0.002
7	0.27±0.71	1.29±1.97	0.012
Probing depth (mm)			
60	3.12±1.16	3.25±1.22	0.164
PCOQ			
14	18.7±6.89	24.3±6.18	0.010

Values are presented as mean±standard deviation

Table 2. Comparison of postoperative evaluation parameters between the experimental and control groups.

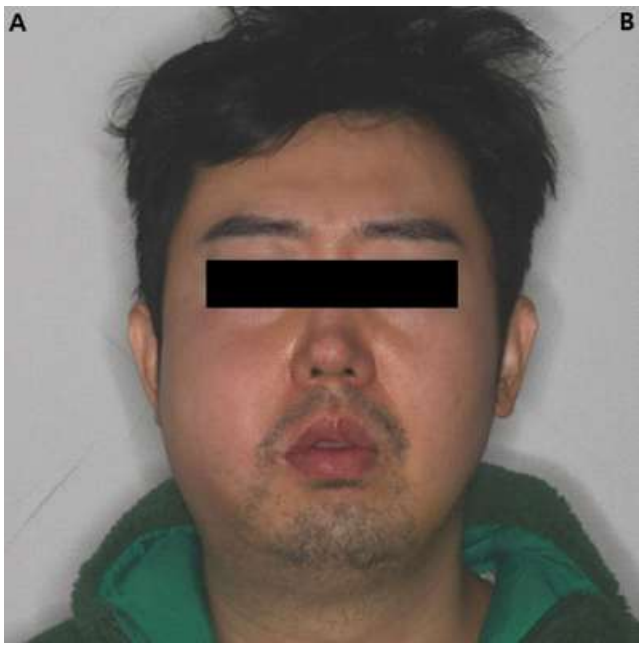


Figure 6. Patient with evident postoperative swelling day 3 on the control side (A) while swelling is not present on the experimental side (B)

4. Discussion

Third molar surgery is frequently associated with various postoperative complications.[31] To minimize these complications and alleviate postoperative pain and swelling, numerous investigations have been made in previous studies to evaluate various interventions such as systemic or localized corticosteroids, natural substances, platelet concentrates, and adjunctive laser therapy after surgical removal of IMTMs.[4),32),33)] In the field of oral surgery, PDRN has only been investigated in animal models to evaluate its efficacy on bone formation after tooth extraction.[10)] Given the preclinical nature of such study, the primary focus was limited to histomorphometric analysis of bone formation rather than clinical parameters such as postoperative complications or soft tissue healing. Therefore, this study is the first to evaluate the efficacy of PDRN on postoperative complications in humans after oral surgery.

The experimental side exhibited statistically verifiable reduction in pain compared to the control side on POD3 and POD7. However, no statistical difference was observed between the two sides in terms of pain duration. This suggests that while patients were able to differentiate the intensity of pain between the right and left sides, it might have been challenging to determine whether the duration of pain was specifically due to the experimental or control side. This may be due to a limitation associated with the nature of split-mouth study design.[34)] In addition, factors such as blood clot formation, the influx of food debris into the extraction socket, and the presence of infection could have influenced both the intensity and duration of pain, regardless of group allocation.[35)] Furthermore, since pain is inherently subjective, both the intensity and duration may vary between individual patients, and there is a limitation of objectively quantifying pain. These factors should be considered when interpreting the results.

In terms of postoperative swelling, the Laskin method was used with a tape by calculating the sum of two linear measurements among defined reference points.[23),36),40)] The linear measurement method is a simple, non-invasive,

reproducible, and inexpensive method to measure the volume of facial swelling.[37] However, since the linear measurement method is dependent on the examiner, it may not be only subjective but also inaccurate due to the errors made in the length measurement procedure. To overcome the limitation of traditional linear measurements, digital software was also used in the current study to quantify and evaluate volumetric differences between the two groups, providing reliable data for objective comparison.[39] The results showed reduction in terms of postoperative swelling on the experimental side. Through the use of CS Face Scan Kit (CS 9600, Carestream Dental LLC. 3625 Cumberland Blvd. Ste. 700 Atlanta, GA 30339 USA) and digital software, volumetric difference between experimental and control groups (PDRN injection after surgery vs Normal Saline injection after surgery) was obtained objectively, not only enhanced the precision and depth of these findings but also provided unprecedented insights into the three-dimensional changes of the face after IMTMs extraction.[38] However, although the digital measurement method is accurate compared to the conventional linear measurement method, its implementation remains limited by the complexity of the equipment use and the high cost of the software.[39]

Measurement of periodontal pocket depth following IMTM extraction is considered a useful indicator for indirectly assessing the periodontal status of surgical site, healing of soft tissues, and alveolar bone. This parameter is particularly valuable when pre-existing periodontal disease or infection is present. In this study, PPD was evaluated at 2month postoperatively in both the experimental and control groups and no statistically significant differences were observed between two groups. These findings suggest that both groups demonstrated comparable levels of soft tissue healing and alveolar bone preservation. Although PDRN have facilitated the early stages of wound healing, its influence on long-term periodontal pocket depth appears to be limited. It is important to note that post extraction pocket depth can be modulated by a complex interplay of biological and mechanical factors. Future investigations incorporating extended follow up durations and radiographic evaluation of alveolar bone regeneration are warranted to more precisely delineate the utility of PDRN in intraoral surgical applications.

In the PCOQ, participants reported a notable improvement on the experimental side in QOL at POD14 after IMTM surgery. In the split-mouth design, patients distinguished the difference between the experimental and control groups in terms of postoperative pain and swelling.[40] However, regarding other PCOQ questionnaires, such as speaking or sleeping, they expressed difficulty in determining whether the discomforts were due to the experimental group or the control group. Moreover, cross-contamination or spilling from one group (experimental or control) could have influenced the other group.[41] Therefore, considering the limitations of the split-mouth randomized controlled trial design, a cautious interpretation of the study outcomes is required. Despite the meaningful clinical outcomes demonstrated in this study, there are several limitations that warrant consideration. First, the absence of histological evaluation limits the findings to fully elucidate the biological mechanisms underlying the effects of PDRN following IMTM extraction. Second, the long-term effects of PDRN on tissue regeneration remain unclear and warrant further investigations through extended follow-up studies. Third, further large-scale studies are required to confirm the findings and validate the results. Additionally, individual variability in healing responses may have influenced the observed outcomes, potentially limiting the generalizability of the results. Moreover, as this study represents a relatively novel application, the dosage reference was limited to previous studies and internal data from Zerone Cellvane, which leads to no study available regarding changes in biological efficacy according to dosage variation.[42),43] Finally, although the study employed a placebo-controlled design, it did not incorporate direct comparison analyses with other regenerative modalities such as platelet-rich plasma, enamel matrix derivative, or hyaluronic acid. Consequently, future studies head-to-head comparisons are required to determine the relative clinical efficacy and therapeutic potential of PDRN in comparison with these established interventions.

5. Conclusion

The present study has shown that PI following IMTM extraction reduced postoperative pain, swelling and patient's discomfort compared to the placebo group. These findings support that the clinical use of PDRN is effective adjunctive therapy for mitigating postoperative complications in oral surgery. Furthermore, this study offers novel clinical insight supporting the potential application of PDRN in oral surgery and emphasizes the necessity for continued research to define its efficacy in postoperative applications.

Supplementary material

Supplementary Table 1
Patient-centered outcome questionnaire(PCOQ), OHIP based version

After third molar surgery					
1. I have experienced oral pain.	1	2	3	4	5
2. I have taken additional analgesics.	1	2	3	4	5
3. I have felt my facial appearance change(swelling).	1	2	3	4	5
4. I have experienced oral bleeding more than 1 day.	1	2	3	4	5
5. I have had an unpleasant taste or fluid in my mouth.	1	2	3	4	5
6. I have noticed a foul odor in my mouth.	1	2	3	4	5
7. I have experienced discomfort while eating.	1	2	3	4	5
8. I have had difficulty articulating words.	1	2	3	4	5
9. I have found it uncomfortable to open my mouth.	1	2	3	4	5
10. I have had difficulty with daily activities.	1	2	3	4	5
11. I have experienced discomfort while attempting to sleep.	1	2	3	4	5

Supplementary Table 1.

Patient-centered outcome questionnaire(PCOQ), OHIP based version

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Abstract in Korean

매복된 하악 제3대구치 발치 후 폴리데옥시리보뉴클레오타이드(PDRN) 의 점막 하 주사의 유효성에 대한 무작위 대조 시험

매복 하악 제3대구치의 외과적 발치는 구강악안면외과 영역에서 가장 보편적으로 시행되는 술식 중 하나로, 점막 골막 피판 절개와 치조골 삭제가 필연적으로 동반되어 연조직의 손상 및 치조골의 흡수가 불가피하다. 이에 따른 수술 후 통증과 부종을 효과적으로 조절하고, 치주조직의 회복을 촉진하여 환자의 삶의 질을 향상시키는 것은 중요하다. 이에 본 연구는 매복 하악 제3대구치 발치 후 폴리데옥시리보뉴클레오타이드의 점막 하 국소 투여가 이러한 임상 지표에 미치는 영향을 평가하고자 수행되었다. 전신질환이 없는 30명의 성인을 대상으로 전향적, 무작위, 분할-구강(split-mouth) 설계 임상시험을 수행 하였다. 모든 피험자에게 동일한 술자가 양측 매복 하악 제3대구치 발치한 후, 시험측에는 폴리데옥시리보뉴클레오타이드를 점막하로 투여하고, 대조측에는 생리식염수를 동일한 방식으로 주입하였다. 주요 평가지표는 수술 후 통증으로 설정하였으며, 시각적 상사 척도(visual analog scale, VAS)를 활용하여 정량적으로 측정하였다. 이차 평가지표로는 선형 계측법 및 안면 스캔을 기반으로 한 3차원 부피 분석을 이용한 안면 부종 평가, 치주낭 깊이 측정을 이용한 치주조직 회복 평가, 그리고 환자 중심 임상결과 설문지(patient-centered outcome questionnaire, PCOQ)를 활용한 환자 보고 결과(patient-reported outcomes, PROs)를 포함하였다. 그 결과, 시험측에서 대조측에 비해 수술 후 통증, 부종, 불편감이 통계적으로 유의하게 감소하였다. 이는 매복 하악 제3대구치 발치 후 폴리데옥시리보뉴클레오타이드의 점막 하 투여가 환자의 수술 후 불편감을 완화하고 삶의 질을 향상 시키는데 기여할 수 있는 잠재적 보조 치료 전략이 될 수 있음을 시사한다. 다만, 본 연구는 단일 기관에서 단일 술자에 의해 수행된 제한된 표본 규모의 임상시험으로, 결과의 외적 타당성을 일반화하기에는 제약이 따른다. 따라서 본 연구 결과의 임상적 신뢰성과 적용 가능성을 보다 정밀하게 검증하기 위해서는 대규모, 다기관, 무작위 대조 임상시험과 장기적 추적 관찰이 병행된 후속 연구가 필요할 것으로 사료된다.

핵심되는 말: 외과적 발치, 폴리데옥시리보뉴클레오타이드, 수술 후 합병증, 무작위 대조 연구