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Early and midterm efficacy of oxiplex gel on postoperative pain intensity, physical disability, and musculoskeletal power in patients undergoing lumbar discectomy

Alireza Tabibkhoeei^{1*} , Maziar Azar¹ , Mohsen Nabiuni¹, Javid Jahandideh², Mohsen Benam¹, Farid Qoorchi Moheb Seraj³, Feizollah Ebrahimnia³ and Ali Moradi^{4,5*} 

Abstract

Introduction Carboxymethylcellulose/polyethylene oxide, also known as Oxiplex gel, is commonly used during lumbar discectomy operations. It serves to cover the surgical site, preventing adhesions and providing relief from pain and symptoms. However, there is ongoing debate regarding the extent of its beneficial effects on postoperative pain intensity, level of disability, and overall improvement of musculoskeletal conditions. Therefore, the objective of this study is to evaluate the advantages and limitations of using Oxiplex gel in lumbar laminectomy procedures specifically for herniated discs.

Methods A randomized controlled trial was conducted on 56 consecutive patients who were candidates for unilateral lumbar discectomy on one lumbar surface. The patients were chosen based on their clinical manifestations and imaging findings. After the initial assessment, the patients underwent either laminectomy or laminotomy surgery. Following the surgery, the patients were randomly assigned to either the intervention group (receiving Oxiplex gel) or the control group. This assignment was done using a computerized random number generator. Assessments were conducted before the operation, as well as 3 and 6 months post-surgery for all patients.

Results There was no significant difference found between the Oxiplex gel and control groups in terms of radicular and low back pain intensity, as well as disability scores, at different time points after surgery ($p=0.336$, $p=0.65$, and $p=0.336$, respectively). Additionally, there were no significant differences found in the prevalence of sexual or sphincteric disorders between the two groups during postoperative assessments ($p=0.639$ and $p=0.15$, respectively). Furthermore, no significant differences were observed in the results of the postsurgical neuromuscular evaluation under different lower extremities conditions between the two groups.

Conclusions Based on our findings, it was observed that Oxiplex gel did not demonstrate any improvement in post-unilateral lumbar discectomy symptoms or musculoskeletal power.

Keywords Discectomy, Laminectomy, Oxiplex/SP

*Correspondence:

Alireza Tabibkhoeei
alireza.tabibkhoeei@gmail.com
Ali Moradi
ralimoradi@gmail.com

Full list of author information is available at the end of the article



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Introduction

Intervertebral disc (IVD) degeneration is one of the main causes of low back pain [1]. The IVD is a functional part of the spine consisting of the annulus fibrosus and nucleus pulposus [2]. The nucleus pulposus has a high concentration of proteoglycan, resulting in a high water content and inflammatory pressure, while the annulus fibrosus is composed of layered collagen fibres [3]. These structural properties of the annulus fibrosus and nucleus pulposus, contribute to both the motion and strength of the IVD, playing a crucial role in the tolerance of body weight.

Approximately 900,000 patients undergo spine surgery in the United States each year [4–6]. After surgery, inflammation, neurotoxin infiltration, and the formation of fibrotic structures in the epidural space can cause both lumbar and leg pain [7]. Many patients require additional surgery for disc herniation due to ongoing or recurring pain even six years after their initial operation. It has been reported that 15.9% of patients with lumbar disc herniation undergo surgery [8]. Over a five-year follow-up period, the overall cumulative rate of re-operation is 11% [9]. Therefore, reducing back and leg pains as well as the rate of recurrence after surgery is a crucial goal in spine surgery.

Fail back surgery syndrome refers to the constant lumbar spinal pain following lumbar discectomy. This condition affects the quality of life for 10–40% of patients [10, 11]. The complexity of the surgery also increases the failure rate for both lumbar discectomy (30–46%) and fusion (19–25%). The pathophysiology of this syndrome involves dural fibrosis, nerve impairment, and disc instability that occur after the operation [12, 13]. Sensory nerve fibers are primarily found on the surface of the annular fibrosis and along the annular gap [14, 15]. Patients with lumbar disc herniation typically have a higher density of sensory nerves in the fibrosis and epidural space compared to those with low back pain [16]. During and after surgery, a variety of pain mediators are associated with sensory nerves. These mediators can sensitize the nerve tissue and lead to neurological symptoms [17]. Additionally, suspended nuclear substances can stimulate the sensory nerves in the epidural space [18, 19]. Increased sensory nerve excitability following surgery often leads to heightened sensitivity and persistent pain [20, 21].

Carboxymethylcellulose/polyethylene oxide (Oxiplex gel) is used during lumbar discectomy operations to prevent adhesions, relieve pain and symptoms, and cover the surgical site [22]. It is applied in the final step of the surgery, just before closing, to provide coverage. Similar to the natural barrier surrounding the nerve root, Oxiplex gel fills the epidural space, annulus fibrosus, and other neural structures, resulting in reduced postoperative pain

by isolating these structures and reducing fibrosis formation and pain mediator production [23]. This study aims to evaluate the benefits and limitations of using Oxiplex gel in lumbar laminectomy for herniated discs.

Materials and methods

Patient selection

The approval to conduct this study was provided by the ethics committee of Iran University of Medical Sciences (IR.IUMS.FMD.REC 1396.9211255001). The study was also registered at the Iranian Registry of Clinical Trials (IRCT20171124037606N1). All patients who were referred to Rasoul-e-Akram Hospital and met the criteria for unilateral lumbar discectomy on one lumbar surface based on their clinical manifestations and imaging findings (magnetic resonance imaging (MRI)) were enrolled in this randomized, double-blind, single-center controlled trial.

The study included patients who experienced severe pain while sitting and getting up, as well as muscle spasms and limited movement. Confirmation of disc herniation, extrusion, or sequestration was done through MRI, CT-scan, or myelogram. Motor assessment, urological and sexual function assessment, as well as musculoskeletal and neurological assessments were also conducted.

Patients who had taken corticosteroids or undergone lumbar puncture in the week leading up to the surgery, as well as those with intervertebral stenosis and/or simultaneous surgeries involving repair of dura rupture, multilevel herniation, opposite exploration, or fat placement on the dura, were not included in the study.

Participants who met the eligibility criteria were randomly assigned to either the intervention or control groups using a computerized random number generator. After undergoing laminectomy or laminotomy surgery, the patients in the intervention group had 3 ml of Oxiplex gel (FzioMed Inc., San Luis Obispo, CA) applied to both the annulus fibrosus and nerve root before closure. Routine closure was performed for all patients, and the operations were conducted by a single surgeon. To maintain blinding, strategies were implemented to ensure that none of the patients, the person conducting the evaluations and assessments, or the physician in charge of the physical examination were aware of the surgical procedure or the application of Oxiplex gel.

Patients follow up

Examination and symptom severity

All patients were visited by a neurosurgeon who was unaware of their medical history at our tertiary hospital, specifically the Neurological Surgery Clinic. These visits took place during the first, third, and sixth months after their operation. During these visits, the patients underwent

neurological examinations to assess for any central spinal fluid (CSF) leakage, bleeding or swelling at the site of the operation, as well as any back pain, radicular pain, or changes in their level of disability.

Symptom severity was evaluated using the visual analogue scale (VAS) and the Oswestry Disability Index (ODI). The patients, interviewer, surgeon, and study analyzer remained unaware of the patients' treatment status until the study concluded. After discharge, all patients were contacted via phone calls or emails and asked to complete self-assessment questions. Physical examinations, as well as musculoskeletal and neurological assessments using the VAS and ODI scoring systems, were conducted at three and six months post-surgery.

Imaging

A 1.5 T MRI of the lumbar spine was conducted for all patients enrolled in two study groups. The MRI utilized a standard protocol turbo spin echo (TSE) or fast spin echo (FSE) sequence, capturing both sagittal and axial T1 and T2 weighted images. The purpose of the MRI was to assess disc degeneration, bulging discs, osteophytes, intra-facet effusion, and paraspinal muscle dimensions before surgery and at the twelve-month follow-up. A masked neuroradiologist visually analyzed the baseline and follow-up MRI scans of the patients' data.

Statistical analysis

Data analysis was conducted using SPSS software version 23.0 for Windows (IBM, Armonk, New York). Quantitative variables are presented as mean \pm standard deviation (SD), while categorical variables are summarized by frequency (percentage). The student t-test was used to compare continuous variables, while the Mann–Whitney test was used for non-normally distributed data or when the assumption of equal variances was violated across the study groups. The chi-square test was used to compare categorical variables. The statistical significance level was set at $p \leq 0.05$.

Results

In this study, a total of 56 consecutive patients were enrolled. Among them, there were 36 males (64.36%) and 20 females (35.67%). The mean age of the participants was 44.63 ± 1.63 years old. The patients had an average BMI of 25.77 ± 2.71 , with 20 individuals (35.71%) classified as overweight and 8 individuals (14.28%) classified as obese. The average duration of low back pain prior to surgery was 7.81 ± 1.18 months. Additionally, a higher incidence of intervertebral disc involvement was observed between the 4th and 5th lumbar spine vertebrae. The patients were divided into two groups, with

28 participants in each. They were randomly assigned to either the Oxiplex group or the control group.

The two groups had similar baseline characteristics, including age ($p=0.315$), weight ($p=0.954$), height ($p=0.977$), gender ($p=0.451$), and history of diabetes ($p=0.639$), sexual disorders ($p=0.639$), and sphincteric disorders ($p=0.15$). There were also no significant differences in baseline radicular pain ($p=0.953$) and positive straight leg raise test ($p=0.982$) between the two groups (see Fig. 1).

The two groups were also similar in terms of baseline sensory abnormalities, such as hypoesthesia ($p=0.725$), intermittent pain ($p=0.771$), and claudication ($p=0.299$). Additionally, there were no significant differences in pre-operative radiological findings between the two groups (Table 1). Dynamic X-ray radiographies were performed before and during surgery. The operation set for patients with suspected need for facet fusion was made standby available. However, none of our suspected patients were in need for facet fusion surgery. Discectomy was performed using Oxypex gel whenever unstable facets were not seen.

The neurological examination results at all visits are presented in Fig. 2. While there were significant reductions in radicular pain and disability after unilateral lumbar discectomy for all patients, there was no significant difference in radicular pain ($p=0.336$), low back pain ($p=0.65$), and disability ($p=0.336$) between the two groups at different time points following the surgery (Fig. 2-A–C).

The musculoskeletal assessment under various lower extremity conditions (hip flexor and extensor, knee flexor and extensor, ankle dorsi flexor and ankle plantar flexor, and flexor and extensor hallucis longus) showed slight improvement during the follow-up period, but no significant difference was observed between the two groups (Table 2).

During the first year of follow-up, the post-operation MRI showed no evidence of disc extrusion, bulging, or herniation. Additionally, we did not observe any CSF leakage, swelling, or bleeding from the surgery site during the follow-up period. There were no complications that required further disc surgery (Fig. 3).

The sensory neuron assessment could not demonstrate any sensation differences at various time points before and after surgery (Fig. 1).

Discussion

This clinical trial aimed to assess the effectiveness of Oxiplex gel in reducing post-surgical pain and disability, as well as improving musculoskeletal power and sensory condition in patients undergoing unilateral lumbar discectomy. However, our findings revealed no significant

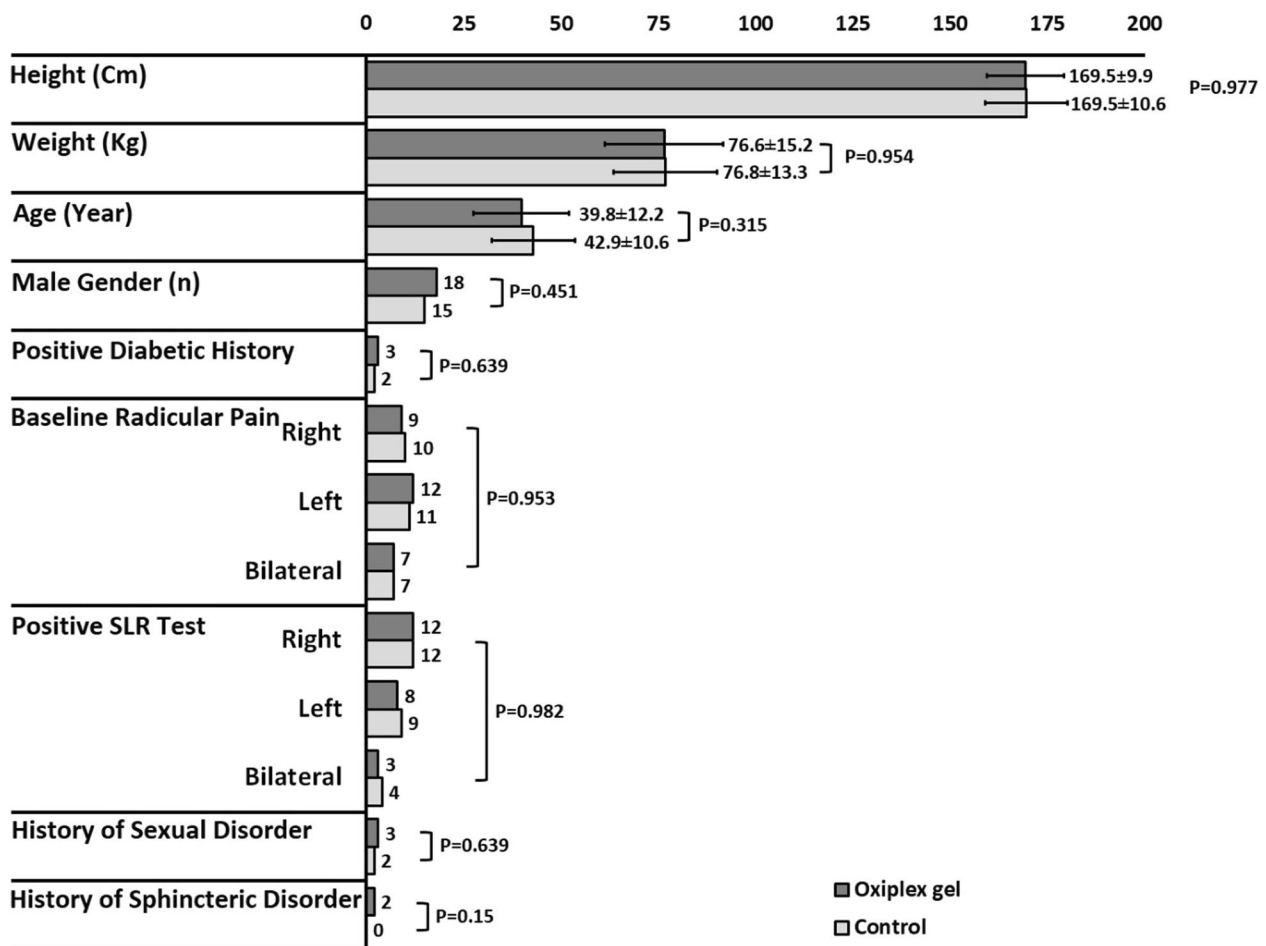


Fig. 1 Baseline characteristics of the Oxiplex gel and control groups

Table 1 Comparison of pre-operative radiological findings between the two groups

	Control	Oxiplex	P-value
Pain duration (month)	11.19 ± 2.33	7.61 ± 0.88	0.667
Herniation level			0.276
L4–L5	16 (28.57%)	15 (26.78%)	
L5–S1	10 (17.85%)	15 (26.78%)	
Osteophyte in vertebral body	16	15	0.276
Degeneration in adjacent disc	24	29	0.446
Suspected for facet fusion	8	8	0.565
Paraspinal muscle (area)	1979.88 ± 55.61	2000.03 ± 390.52	0.874
Disc height	2.70 ± 0.53	2.82 ± 0.51	0.138

impact of Oxiplex gel on these parameters. No adverse events or complications occurred in patients during or after the intervention. Nonetheless, it is important to

note that our study had limitations, such as the lack of MRI evaluation for adhesions in the study population and the fact that we only conducted short-term follow-up.

Oxiplex gel has been claimed to reduce postsurgical adhesions, pain, and disability. However, there have been conflicting results regarding the effectiveness of applying Oxiplex gel to the surgical site [24, 25]. A study conducted by Rhyne et al. showed a significant decrease in postoperative pain intensity when using Oxiplex gel after discectomy. On the other hand, a separate study by Liu et al. found no significant impact on the average VAS and ODI scores in patients who received the gel [15, 26]. While it is important to acknowledge the significant role that Oxiplex gel plays in reducing posterior dural adhesion, its impact on postoperative pain severity may not be substantial. The positive effect of using this gel in conjunction with 1 mg of epidurally administered morphine has only been observed during the initial 36-h post-surgery period [27]. However, other studies have reported long-term benefits for it. Assietti et al. found that Oxiplex

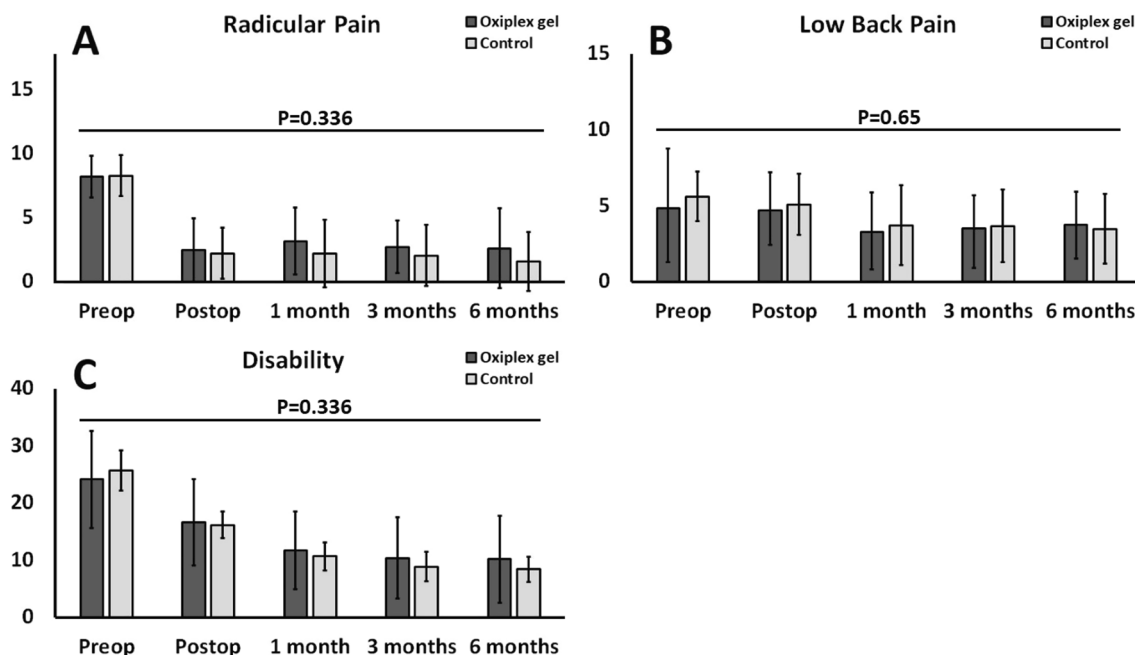


Fig. 2 Neurological examination for radicular pain, low back pain, and disability among the two study groups

gel resulted in a significantly greater reduction in disability (ODI) three years after surgery compared to the control group [18]. Furthermore, the use of Oxiplex gel in treatment showed a significant increase in the number of patients who experienced no disability (0% ODI). In addition, compared to the control group, patients treated with Oxiplex gel reported a greater reduction in both leg and back pain. These findings are consistent with a study conducted by Kim et al., which demonstrated that patients with severe leg pain and lower-extremity weakness who received Oxiplex gel experienced decreased symptoms as assessed by the lumbar spine outcome questionnaire at 30 days, 90 days, 6 months, and 12 months post-discectomy, when compared to control patients who did not receive Oxiplex gel [28]. Additionally, there was no notable difference in the MRI abnormality score between the two groups after a period of three months.

The manufacturers claim that there would be no post-operative CSF leakage and fewer reoperations. However, it's important to note that we observed no instances of CSF leakage or reoperation in either group of our study. Additionally, patients reported increased satisfaction due to reduced leg and back pain. However, we did not measure the quality of life in our population after Oxiplex gel injection or in our control group. A systematic review by Hosseini et al. demonstrated that antiadhesive gel has an effect on leg pain but not on low back pain.

Table 3 shows the reoperation rates of previous studies at various time points [18, 20, 29].

All MRI imaging revealed no signs of herniation or disc extrusion after the unilateral discectomy. In a study conducted by Fransen involving 396 consecutive patients who used carboxymethyl cellulose/polyethylene oxide as an antiadhesive, six instances of disc reoperation were observed, which were attributed to infection and disc reherniation. The majority of these cases occurred during the initial phase following the discectomy [30]. However, this argument may be attributed to the different populations in the two studies. Nonetheless, it is worth noting that no reoperations were scheduled for our study patients within a 12-month follow-up period after the administration of Oxiplex gel. The lower rate of reoperations observed in the Oxiplex gel groups in various studies, along with its ease of application and minimal occurrence of adverse events, indicates the favorable use of Oxiplex gel (Table 3).

The discrepancies in outcomes among different studies may be due to several factors, including the quality of the surgical procedure, the imaging techniques used to evaluate patients after surgery, the duration of the follow-up period, and the variation in the questionnaires used to assess pain. Although the Lumbar Spine Outcomes Questionnaire (LSOQ) has been utilized in these studies, it is worth noting that most studies investigating anti-adhesion gels such as Oxiplex[®], Adcon-L[®] (Gliatech Inc., Cleveland, OH), Healon-GV[®] (Pharmacia & Upjohn, Kalamazoo, Michigan), and DuraSeal[®] Xact (Covidien Inc., Mansfield, MA) have reported

Table 2 Comparison of musculoskeletal assessment of right and left leg between the two groups

	Preop	Postop	1-month	3-months	6-months	P
HF						
Right, Oxiplex gel	4.89±0.31	4.92±0.26	5.00±0.01	5.00±0.01	5.00±0.01	0.282
Control	4.96±0.18	5.00±0.01	5.00±0.01	5.00±0.01	5.00±0.01	
Left, Oxiplex gel	4.85±0.35	4.89±0.31	5.00±0.01	5.00±0.01	5.00±0.01	
Control	4.92±0.26	4.96±0.18	5.00±0.01	5.00±0.01	5.00±0.01	
HE						
Right, Oxiplex gel	4.89±0.31	4.92±0.26	5.00±0.01	5.00±0.01	5.00±0.01	0.282
Control	4.96±0.18	5.00±0.01	5.00±0.01	5.00±0.01	5.00±0.01	
Left, Oxiplex gel	4.85±0.35	4.89±0.31	5.00±0.01	5.00±0.01	5.00±0.01	
Control	4.92±0.26	4.96±0.18	5.00±0.01	5.00±0.01	5.00±0.01	
KF						
Right, Oxiplex gel	4.82±0.35	4.89±0.31	5.00±0.01	5.00±0.01	5.00±0.01	0.611
Control	4.85±0.35	4.96±0.18	5.00±0.01	5.00±0.01	5.00±0.01	
Left, Oxiplex gel	4.82±0.39	4.85±0.35	5.00±0.01	5.00±0.01	5.00±0.01	
Control	4.85±0.35	4.92±0.26	5.00±0.01	5.00±0.01	5.00±0.01	
KE						
Right, Oxiplex gel	4.89±0.31	4.89±0.31	5.00±0.01	5.00±0.01	5.00±0.01	0.309
Control	4.96±0.18	4.96±0.18	5.00±0.01	5.00±0.01	5.00±0.01	
Left, Oxiplex gel	4.85±0.35	4.85±0.35	5.00±0.01	5.00±0.01	5.00±0.01	
Control	4.92±0.26	4.92±0.26	5.00±0.01	5.00±0.01	5.00±0.01	
ADF						
Right, Oxiplex gel	4.82±0.94	4.82±0.94	5.00±0.01	5.00±0.01	5.00±0.01	1.000
Control	4.82±0.94	4.82±0.94	5.00±0.01	5.00±0.01	5.00±0.01	
Left, Oxiplex gel	4.78±0.49	4.92±0.26	4.96±0.18	4.96±0.18	4.96±0.18	
Control	4.85±0.44	4.92±0.26	4.96±0.18	4.96±0.18	4.96±0.18	
APF						
Right, Oxiplex gel	4.85±0.75	4.82±0.94	5.00±0.01	5.00±0.01	5.00±0.01	1.000
Control	4.85±0.75	4.82±0.94	5.00±0.01	5.00±0.01	5.00±0.01	
Left, Oxiplex gel	4.92±0.26	4.92±0.26	5.00±0.01	5.00±0.01	5.00±0.01	
Control	4.92±0.26	4.92±0.26	5.00±0.01	5.00±0.01	5.00±0.01	
EHL						
Right, Oxiplex gel	4.53±1.20	4.64±1.19	5.00±0.01	5.00±0.01	5.00±0.01	0.759
Control	4.42±1.19	4.64±1.19	5.00±0.01	5.00±0.01	5.00±0.01	
Left, Oxiplex gel	4.71±0.65	4.78±0.49	4.89±0.41	4.89±0.41	4.89±0.41	
Control	4.57±0.83	4.78±0.49	4.89±0.41	4.89±0.41	4.89±0.41	
FHL						
Right, Oxiplex gel	4.67±1.02	4.75±1.00	4.82±0.54	4.85±0.52	4.85±0.52	0.650
Control	4.64±1.02	4.75±1.00	4.78±0.56	4.85±0.52	4.85±0.52	
Left, Oxiplex gel	4.82±0.39	4.82±0.39	4.85±0.44	4.85±0.44	4.85±0.44	
Control	4.78±0.41	4.78±0.49	4.85±0.44	4.85±0.44	4.85±0.44	

HF: hip flexor, HE: hip extensor, KF: knee flexor, KE: Knee extensor, ADF: ankle dorsi flexor, APF: ankle plantar flexor, FHL: flexor hallucis longus, and EHL: extensor hallucis longus

significant reductions in leg pain according to VAS scales (-0.53 versus -0.08 , 95% CI -0.86 , -0.20), as compared to studies employing the LSOQ [18, 28, 29, 31, 32]. Dural adhesions may still occur up to seven months after surgery. Therefore, it is recommended to perform an MRI to evaluate fibrosis following the

surgery [21]. The outcome measurements in both short-term and long-term investigations may be influenced by differences between the two groups [33]. To confirm the effectiveness of anti-adhesion medications in reducing pain severity, further studies with larger sample sizes and longer follow-up times are necessary.

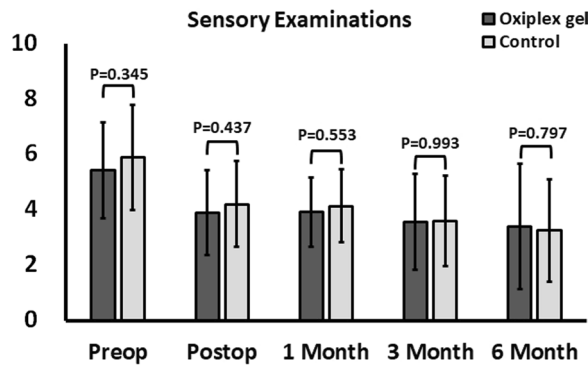


Fig. 3 Sensory neuron assessment at various time points before and after surgery

Table 3 Comparison of reoperation rates in various studies

	Reoperation rate (%)	
	Oxyplex gel	Control
Assietti et al. (6 month follow up)	0	5.7
Rhyne et al. (36 month follow up)	0.6	3.4
Current study (12 month follow up)	0	0

Conclusion

According to the findings of the current study, covering both the annulus fibrosus of the dura and nerve root with 3 ml Oxiplex gel before routine closure resulted in no symptom alleviation in patients undergoing laminectomy or laminotomy surgeries. Further studies should be performed to elucidate the efficacy of separating gels in pain and symptom reduction in laminectomy surgeries.

Abbreviations

ADF	Ankle dorsi flexor
APF	Ankle plantar flexor
BMI	Body mass index
CSF	Central spinal fluid
EHL	Extensor hallucis longus
FHL	Flexor hallucis longus
FSE	Fast spin echo
HE	Hip extensor
HF	Hip flexor
IVD	Intervertebral disc
KE	Knee extensor
KF	Knee flexor
LSOQ	Lumbar Spine Outcomes Questionnaire
MRI	Magnetic resonance imaging
ODI	Oswestry Disability Index
Oxiplex gel	Carboxymethylcellulose/polyethylene oxide
TSE	Turbo spin echo
VAS	Visual analogue scale

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Author contributions

MN: Study conceptualization and drafting the manuscript; FE: data analysis and interpretation, drafting the manuscript; AT: Study conceptualization, data collection; MA: data collection; MB: data analysis and interpretation; JJ: data analysis and interpretation; FQMS: drafting the manuscript; AM: study conceptualization, data analysis and interpretation. All author have read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate:

The approval to conduct this study was provided by the ethics committee of Iran University of Medical Sciences (IR.IUMS.FMD.REC 1396.9211255001). The study was also registered at the Iranian Registry of Clinical Trials (IRCT20171124037606N1).

Consent for publication

The authors declare no conflict of interest regarding this manuscript and no conflicts of interest with any companies or distributors involved in the production or distribution of Oxiplex.

Competing interests

The authors declare no competing interest regarding this manuscript and no competing interest with any companies or distributors involved in the production or distribution of Oxiplex.

Author details

- ¹Department of Neurosurgery, Iran University of Medical Sciences, Tehran, Iran.
- ²Department of Neurosurgery, Qazvin University of Medical Sciences, Qazvin, Iran.
- ³Section of Neurovascular Intervention, Neurosurgical Department, Ghaem Hospital, Mashhad University of Medical Sciences, Mashhad, Iran.
- ⁴Clinical Research Development Unit, Ghaem Hospital, Mashhad University of Medical Sciences, Ahmad-Abad Street, Mashhad 9176699199, Iran.
- ⁵Orthopedic Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.

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