MMSL Military Medical Science Letters Since 1925

Mil. Med. Sci. Lett. (Voj. Zdrav. Listy) 2025, 94(1), 2-9
ISSN 2571-113X (Online)
DOI: 10.31482/mmsl.2023.044

ORIGINAL ARTICLE

A POSSIBLE EFFECT OF EPIDURAL STEROID INJECTION ON COLLAGE TYPE II –α1 LEVEL IN PATIENTS WITH LOW BACK PAIN

Zainab R. Alqaseer [1], Ajil A. Alzamily [1]✉, Raad A. Alkhafaji [2], Emad M. Hussain [2], Thaier A. Alkhafaji [2]

[1] College of Medicine, University of AL-Qadisiyah; Al-Diwaniyah, Iraq
[2] Diwaniyah Health Department; Al-Diwaniyah Teaching Hospital, Al-Diwaniyah, Iraq

Received 7th May 2023.
Accepted 15th December 2023.
Published 3rd March 2025.

Summary

Background: Low back pain (LBP) is one of the common muscloskeletal diseases and usual treated by epidural steroid injection (ESI). ESIs improve patients' quality of life, reduce lumbar radicular pain, and postpone spinal surgery. The mechanism of improvement is yet unscertain, perhaps involve type α collagen (COL2α) for bone maintenance, hence, we sought to investigate the role of injected steroids in bone healing focusing on the role of COL2α.

Methods: All patients in this research were diagnosed by specialists based on their histories and clinical features and associated diseaeses or compiling therapy. Serum samples collected from LBP patients and control group for comparisons.

Results: The present study found a significant (<0.0001) increase in the concentration of COL2α in patients with LBP after injection with ESI treatment compared with patients before injection and healthy individuals.

Conclusion: ESI helps LBP sufferers by boosting COL2α, which repairs damaged tissues.

Key words: Steroids; Epidural injection; Collagen 2α; Low back pain; Lumbar radicular pain

Introduction

Lumbar radicular pain (LRP) and low back pain (LBP) are frequent causes of physical and mental illness and substantial economic costs (1). LBP is also known as sciatica, lumbosacral radicular syndrome, lumbar radiculopathy, nerve root discomfort, or nerve root irritation in the medical literature. Most people report it as a backache that radiates to their legs (2). First is intervertebral disk disease. Intervertebral disk disease may induce disk herniation, degenerative diseases including channel stenosis, or persistent instability in afflicted segments. Sciatica is most often caused by lumbar nucleus pulposus herniation, which causes stenosis and irritation (3, 4).

Collagen type II alpha 1, commonly referred to as COL2α1, is a significant human gene that plays a crucial role in the creation of type II collagen's pro-alpha1(II) chain. This gene encodes a protein that provides structural support

✉ University of AL-Qadisiyah; College of Medicine, Al-Diwaniyah, Iraq
ajil.alzamily@qu.edu.iq
☎ +9647810624784

to various tissues in the body, including cartilage and the vitreous fluid of the eye. Type II collagen is a fibrillar collagen that is primarily found in cartilage, which is a connective tissue that cushions and protects the joints from damage caused by friction and pressure. The collagen fibres provide strength and stability to the cartilage, allowing it to withstand the forces exerted on it during movement. (5, 6). Achondrogenesis, chondrodysplasia, early-onset familial osteoarthritis, and SED congenital are all linked to mutations in this gene. This gene has two distinct transcripts (7, 8). Type II collagen gives structure and strength to cartilage, the jelly-like eyeball filling (vitreous), the inner ear, and spinal discs (nucleus pulposus). Active discopathy reduces chondrogenesis transcription factors such as type 2 collagen(9). CT-II showed that osteochondrosis was associated with enhanced cartilage catabolism, which shows that osteochondrosis is significantly linked to increased cartilage catabolism (10).

In the present study, we aimed to investigate into the role of injected steroids in bone healing, with a particular focus on the involvement of COL2α. Bone healing is a complex process that involves various factors, and understanding the mechanisms behind it is crucial for developing effective treatment strategies. Steroids have been widely used in the medical field for their anti-inflammatory and immunosuppressive properties. However, their impact on bone healing remains a topic of debate and investigation. By exploring the specific role of COL2α, a protein that plays a vital role in the formation and maintenance of cartilage and bone, we aimed to shed light on the potential influence of injected steroids on bone healing at a molecular level. This investigation is crucial as it can help guide clinicians in making informed decisions regarding the use of steroids in bone healing scenarios, ultimately leading to improved patient outcomes.

Patients and Methods

A total of 58 individuals (36 healthy control group and 22 diagnosed LBP Patients) enrolled in this study. Ages, genders, height, and weight were recorded.

Exclusion criteria include patients with acute or chronic liver illness, kidney disease, thyroid function issues, diabetes mellitus, hypertension, COVID-19, and autoimmune diseases.

A formal consent has signed by each participant in this study.

Serum collected from participants and analysed for measurement of COL2α1 (Elabscience® ELISA kits as per manufacturer instruction). To measure COL2α1, samples or standards loaded to the wells of the micro ELISA plate. Then, in a mesmerizing sequence, combined them with a biotinylated detection antibody designed exclusively for human COL2α1, followed by the addition of the Avidin-Horseradish Peroxidase (HRP) conjugate. After a brief period of incubation, any free components were washed away, leaving behind only the bound human COL2α1, biotinylated detection antibody, and Avidin-HRP conjugate. The wells that contain this combination developed blue color by the addition of the substrate solution. Followed by addition of the stop solution , causing the color to transform into a yellow. The sampleswere then quantified by measuring the optical density (OD) spectrophotometrically at a wavelength of 450 nm.

Statistical Analysis: GraphPad Prism 9.2.0 and Excel 2013 were used to summarize, analyze, and display data. Data were expressed using mean and standard deviation. Categorical data were also numbered. Regularly distributed variables were compared using one-way ANOVA and an unpaired t-test. Chi-square tested qualitative data. Bivariate correlation utilized Pearson's coefficient. p-value >0.05 was significant.

Results

The results of this study show mean age of patients with low LBP was 50.36±13.13 years, while the age of control was 37.19±7.596 years. There was a highly significant difference in the mean age between LBP and control (p-value < 0.0001) (Table 1).

The body mass index (BMI) (kg/m^2) of patients with LBP was calculated at (28.34±5.260) (kg/m^2), while that of control was (24.03±1.786) (kg/m^2) and was a significant difference in BMI (Table 1).

The results of this study showed decreased levels of COL2α (28.91±7.939) ng/mL in patients with LBP as compared with after injection and control, (41.24±7.968), (45.09±7.530), ng/mL, respectively; The results of our study have shown high significant difference (p-value < 0.0001) in the concentrations of COL2α as compared patients with LBP and Control. Also, a significant difference was present in mean values after injection and before injection (p-value = 0.0007). A substantial difference in mean values before injection and control (p-value < 0.0001), but there is a non-significant in mean values after injection and control (p-value = 0.2733) (Table 1).

Table 1. Characteristics of LBP and Control.

Characteristic	Patients n=22		Control n=36	*P-value*
	Before	After		
Age				
Range	30 – 79		30 - 60	<0.0001
Mean ± SD	50.36 ± 13.13		37.19 ± 7.596	
BMI (kg/cm²)				
Range	21.78 - 46.48		**20.45 - 26.81**	**<0.0001**
Mean ± SD	28.34 ± 5.260		24.03 ± 1.786	
COL2α1 (ng/mL)				
Range	14.98 - 40.22	23.34 - 50.43	13.85 - 56.58	<0.0001
Mean ± SD	28.91 ± 7.939	41.24 ± 7.968	45.09 ± 7.530	

n: number of cases; SD: standard deviation; BMI: Body mass index COL2α1: Collagen Type II Alpha 1. As described above, there was a significant elevation in the COL2α1 levels in LBP patients after ESI as compared with patients before injection and controls.

Ageing has significantly decreased the amount of collagen precipitated locally with the use of ESI compared to the control group (Figure 1). Moreover, the responsiveness of collagen precipitated locally is reduced with ageing (Figure 2).

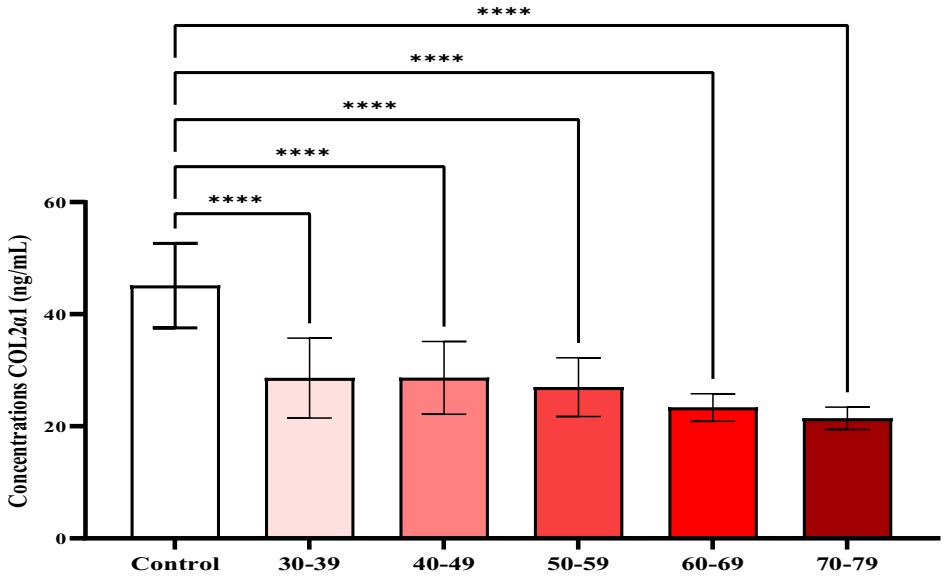

Figure 1. Estimation of concentrations of collagen type II alpha 1 [COL2α1 (ng/mL)] A comparison between control and patients among different age groups showed the presence of a significant decrease (P<0.0001) in the patient's group to control in all age subgroups. Data are expressed as means ± SD. Indicates ****significant differences compared to the Control, P≤0.05.

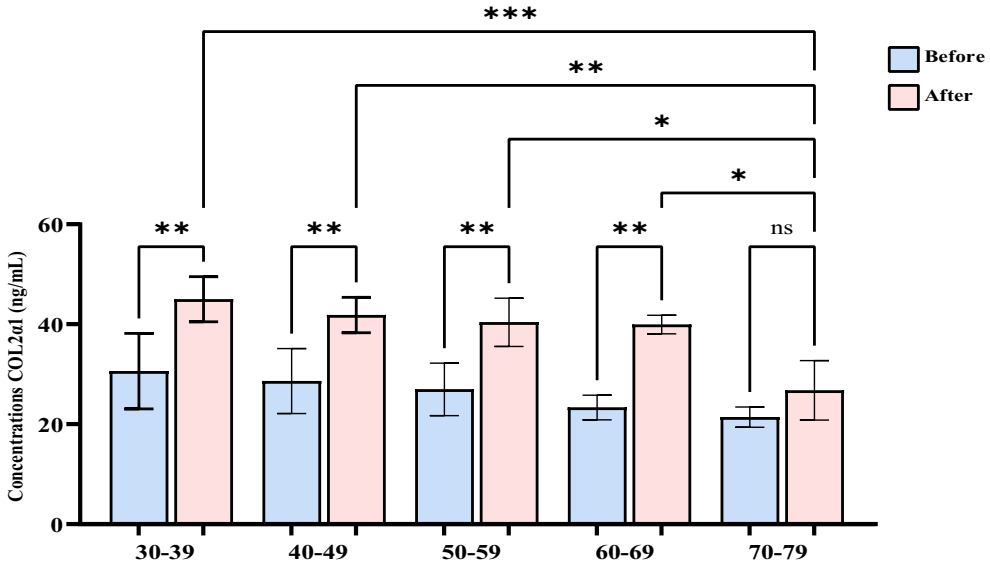

Figure 2. Estimation of serum concentrations of collagen type II alpha 1 [COL2α1 (ng/mL)] after the ESI among the different groups. Data are expressed as means ± SD. * *p-value* ≤0.05,** *p-value* ≤0.001 and *** *p-value* ≤0.0001.

After the injection, there was a significant increase in the serum concentration of COL2α1. However, attention was significantly lower in the (70-79) age group than in other groups indicating a slow improvement for older patients. Data are expressed as means ± SD. * *p-value* ≤0.05,** *p-value* ≤0.001 and *** *p-value* ≤0.0001 (Figure 3).

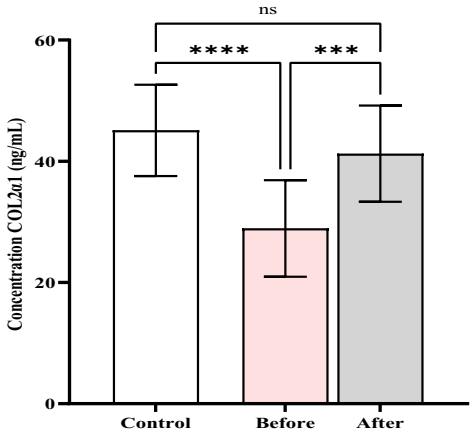

Figure 3. Estimation of serum concentrations of collagen type II alpha 1 [COL2α1 (ng/mL)] after the ESI. Data are expressed as means ± SD. *** *p-value* ≤0.0001.

There was a significant increase (P=0.0007) in the serum concentration of COL2α1 compared to before the injection epidural. However, the concentration was significantly (P<0.0001) than the control.

Discussion

It is noteworthy that as people become older, both the incidence and prevalence of severe and chronic LBP rise (11). The previous study showed that most LBP in elderly people is non-specific and pathology-free (such as a fracture or inflammation) (12). While previous research found that older patients with non-specific LBP may feel pain in various tissues, many older patients with chronic LBP had physical features comparable to sacroiliac joint

pain (83.6%) and myofascial pain (95.5%)(13). Although chordoma, plasmacytoma, and lymphoma are examples of primary malignant tumours that can develop in older persons, the prostate and kidney are the two most well-known metastatic causes of LBP (14). The findings of other studies found that lower education levels, lower income, and smoking are related to a higher propensity of LBP in older people (15-17).

Compared to the control group, individuals with LBP had a higher mean BMI. The average BMI of research participants was 28.34 kg/m^2. Due to the frequency and cost of LBP and obesity, several researchers have investigated their possible link (18, 19). Many studies have concluded that increased BMI is a risk factor for LBP (20, 21). Patients who were discharged from the hospital with a herniated disc diagnosis also had higher BMI rates (22).

Other hypothesized reasons include psychological effects brought on by negative body shape, decreased exercise, systemic inflammation brought on by the production of adipocytokines, and atherosclerosis, which reduces blood flow and nutrients to the discs (23). hs-CRP, TNF, and IL-6 were examined in obese and non-obese adults. Higher levels of back-pain-causing inflammatory mediators were linked to obesity and BMI (24). More recent research suggests that a persistent systemic inflammatory state is the cause of the association between an elevated BMI and LBP and other musculoskeletal pain syndromes, calling for a closer look at this link (25, 26).

Obesity is linked to several diseases, including LBP, headaches, fibromyalgia/chronic generalized pain, and abdominal pain (27). Severe obesity in the elderly doubles the likelihood of having chronic pain (28). People reporting widespread pain tend to have greater total fat mass and less lean mass than those not reporting pain (29).

Collage Type II Alpha I (COL2α) is part of type 2 collagen essential for bone development. COL2α is expressed in the annulus fibrosus and nucleus pulposus (30). It is a minor component of human cartilage but necessary for forming cartilage collagen. Although COL2α fragments accumulate in the degenerative Intervertebral disc (IVD), little is known about how they affect the degenerative process (31).

Our findings showed that in LBP patients before receiving an ESI, COL2 levels were reduced. TNF-a and IL-1, which can cause disc degeneration by reducing anabolic ECM proteins like aggrecan and COL2 and increasing catabolic enzymes like a disintegrin and metalloproteinase with thrombospondin motifs (ADAMTS)-4 and -5 and matrix metalloproteinases, may be responsible for these decreased levels of COL2 (MMPs)(32,33).

According to our research, ESI patients with LBP had higher levels of COL2 than LBP patients without epidural injections or healthy people. A minimally invasive treatment known as an ESI may be used to treat neck, arm, back, and leg pain brought on by irritated spinal nerves as a result of spinal stenosis or disc herniation (1). Our data were incompatible with the results of another study which demonstrated that collagen synthesis was suppressed only by long-term administration of systemic doses of Depo-Medrol® (34). None of the studies conducted in the past estimate elevated levels of COL2α after ESI. Variation in the efficacy of the injected steroids connoted to the reciprocal status of localized cellular milieu including the cytokine-based cellular responsiveness and their correlation with collagen (35, 36). To overcome the limitation of effectiveness, orthopeditian add an adjuvant anti-inflammatory medication, such as risperidone or carbamazepine (37, 38)

However, steroids affect COL2α synthesis, material strength, and tissue healing (39). No difference in COL2α ultrastructure was observed, leading the authors to conclude that anabolic steroids may not induce ultrastructural collagen changes in humans (40). Defects brought on by the loss or fragmentation of collagen in the injured area may be made up for by stimulating de novo COL2 production. This newly generated collagen can be built up to strengthen the harmed tissues' structural integrity and encourage fibroblasts to make additional collagen (41).

Conclusion

In conclusion, epidural steroid injection is an effective treatment for low back pain that positively impacts patients by increasing their COL2α levels. This increase in COL2α levels leads to an improvement in damaged tissue repair and regeneration, resulting in a reduction of pain and an improvement in overall quality of life. ESI is a safe and minimally invasive procedure that is suitable for most patients with low back pain. Therefore, patients with chronic low back pain should consider ESI as an option for pain relief and tissue repair.

Acknowledgement

The authors are grateful to the University of Al-Qadisiyah/College of Medicine for their provided facilities to accomplish this study.

Conflict of interest

The authors declare no conflict of interest concerned in the present study.

Adherence to Ethical Standards

The study was approved by the Research Ethical Committee and Scientific Committee in Al-Qadisiyah, Iraq (Approval Letter No. 11/1000 on 08.03.2022).

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