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The Correlations of IL-1β/IL-10 Ratio and Pain Severity Scale with Histopathological Features of Facet Joint Osteoarthritis in Lumbar Spinal Canal Stenosis Patients

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ABSTRACT

Background: Facet joint osteoarthritis represents the ultimate phase of spinal degenerative disease. Pain can arise from degenerative processes and the presence of inflammatory cytokines in the facet joints. The researchers aimed to investigate the correlation between the IL-1β/IL-10 ratio and pain severity, along with the histopathological characteristics of osteoarthritis in the facet joint of patients with lumbar spinal canal stenosis. The objective was to identify the specific IL-1β/IL-10 ratio that significantly contributes to the development of osteoarthritis.

Methods: The study employed an analytical cross-sectional design and utilized a successive sampling method to select patients with lumbar spinal canal stenosis who matched the specified inclusion criteria. Facet samples were collected to assess the levels of IL-1β and IL-10, the patient's pain intensity, the IL-1β to IL-10 ratio, and the degree of osteoarthritis in the facet joints through histological examination.

Results: Thirty-eight patients met the inclusion criteria with an average age of 58 ± 8.93. Average levels of IL-1β 2268.95 ± 862.80 pg/ml, total IL-10 was 1.86 ± 1.68 pg / ml, degree of pain achieved about 5.82 ± 0.56, no OA facet grade 1, 3 samples (7.9%) grade 2, 14 samples (36.8%) degree 3 and a total of 21 samples (55.3%) degree 4. Significant correlation was obtained between the IL-1β/IL-10 ratio, the degree of pain with the histopathological degree of OA of the facet joint with a value of p= 0.02.

Conclusions: There is a correlation between the IL-1β/IL-10 ratio and the degree of pain with the histopathological picture of arthritis of the facet joint in patients with lumbar spinal canal stenosis.

Keywords: Interleukin-10, Zygapophyseal Joint, Osteoarthritis, Pain Measurement, Spinal Stenosis

INTRODUCTION

Osteoarthritis in facet joints signifies the advanced stage of degenerative spinal bone disease. The onset of spinal bone degeneration is marked by disruptions in the intervertebral disc, leading to subsequent damage to surrounding tissues such as ligaments and bones, ultimately culminating in facet joint osteoarthritis.

The reported prevalence of lumbar facet joint pain varies widely in the literature, with less than 5% to over 90% of patients complaining of back pain.[1,2)] Age is strongly linked to the prevalence of lumbar facet joint arthropathy. According to a study, moderate to severe lumbar facet joint arthropathy is found in 36% of adults under 45 years, 67% of adults aged 45-64 years, and 89% of adults aged 65 years and older.[3)] Another study, utilizing lumbar CT scans and X-rays, found that women above 50 years of age are at a higher risk of developing facet joint osteoarthritis than men.[4)]

Cytokines are believed to play a pivotal role in degenerative joint diseases. Some cytokines are considered to be involved in the pathogenesis of facet joint osteoarthritis. Tsuchida et al., in an observational study of IL-6 and IL-8 levels in synovial fluid, concluded that these cytokine levels increase in the blood and synovial fluid of osteoarthritis patients.[5,6)] Research by Igarashi et al. in 2004, examining IL-1β levels in facet joints, found approximately 11% in lumbar disc herniation (LDH) and 21.7% in lumbar spinal canal stenosis (LSCS).[7,8)] It is noteworthy that not only pro-inflammatory cytokines and cartilage-degrading enzymes but also anti-inflammatory cytokines and inhibitors of cartilage-degrading enzymes, including IL-10, play a role in the degenerative process of facet joints. IL-10 is highly effective in suppressing macrophages' ability to release TNF-a, although some other cytokines (IL-1 and GMCSF) are also induced.[9)] Histopathological examinations are not routinely conducted in LSCS cases, but recent research has begun to explore the degree of facet joint damage based on histopathological findings.[10)]

Researchers are interested in investigating the relationship between the IL-1β/IL-10 ratio and pain levels with the histopathological features of facet joint osteoarthritis in patients with lumbar spinal canal stenosis. This exploration aims to determine a meaningful IL-1β/IL-10 ratio leading to facet joint osteoarthritis.

The study aims to determine the relationship between pro and anti-inflammatory cytokine mediators, pain levels, and the histopathological features of facet joint osteoarthritis in patients with lumbar spinal canal stenosis. It is expected to assist in considering anti-inflammatory interventions in cases of lumbar spinal canal stenosis accompanied by facet joint arthritis.

MATERIALS AND METHODS

The research design employed for this study is a cross-sectional analytical study. The research encompasses various variables, with IL-1β/IL-10 ratio and Pain Degree (VAS) acting as independent variables, Histopathological Features of Facet Joints as dependent variables, and several control variables, both internal (e.g., age, BMI) and external (e.g., corticosteroid use, nutrition).

The study was conducted at RSUP Prof. Dr. I.G.N.G Ngoerah, Denpasar Bali, utilizing clinical and laboratory data obtained from secondary sources in patient medical records. The research period commenced in June 2023 and concluded in November 2023, with subsequent phases of data processing, analysis, and reporting. The study population comprised patients diagnosed with lumbar spinal canal stenosis, meeting inclusion criteria such as age over 50 and willingness to participate. Exclusion criteria included conditions like acute or chronic infections, recent ovary

removal, hormonal medication use, corticosteroid use, malignancy, or spinal trauma history.

Data were collected through various instruments, including laboratory results for inflammation markers, Visual Analog Scale (VAS) questionnaire, lumbar MRI, and histopathological examination of facet joints. The research procedure involved patient selection based on diagnostic criteria, pain measurement, laboratory examinations, IL-1β/IL-10 ratio calculation, sample collection for histopathological examination during spinal surgery, and subsequent data analysis. Data analysis included descriptive and inferential analyses, incorporating normality tests and correlation analyses.

Our chosen methodology aims to investigate the relationship between pro and anti-inflammatory cytokines, pain levels, and histopathological features in patients with lumbar spinal canal stenosis. The study anticipates contributing valuable insights to inform anti-inflammatory interventions for cases of lumbar spinal canal stenosis accompanied by facet joint arthritis.

RESULTS

The study involved 38 patients undergoing spine surgery at Prof IGNG Ngoerah Denpasar General Hospital, examining IL-1β and IL-10 levels, pain intensity, and facet joint histopathology. Table 1 outlines the distribution of subjects' characteristics, highlighting age, gender, inflammatory marker levels, pain intensity, and facet joint histopathology grades. Normality tests (Shapiro-Wilk) were then conducted, indicating non-normal distributions for IL-1β, IL-10, and pain intensity but normal distribution for the IL-1β/IL-10 ratio (Table 2).

Table 1. Distribution of Study Subject Characteristics

Variable	Frequency (%) (n=38)	Mean ± Standard Deviation
Age (Years)	-	58 ± 8.938
Gender Male Female	 20 (52.6%) 18 (47.4%)	
IL-1β Level (pg/ml)	-	2268.95 ± 862.80
IL-10 Level (pg/ml)	-	1.86 ± 1.68
Pain Intensity (using VAS)	-	5.82 ± 0.56
Facet Joint Histopathology Grade 1 Grade 2 Grade 3 Grade 4	 0 (0%) 3 (7.9%) 14 (36.8%) 21 (55.3%)	

Table 2. Normality Test Results

Variable	N	P	Description
IL-1β Level	38	0.009	Non-normal distribution
IL-10 Level	38	0.000	Non-normal distribution
VAS for pain	38	0.000	Non-normal distribution
IL-1β/ IL-10 Ratio	38	0.068	Normal distribution

Subsequently, Fisher's Exact test was employed to assess the relationships between IL-1β, IL-10, pain intensity, and facet joint histopathology (Table 3). Significant associations were found between IL-1β level ($p = 0.039$, $r = 0.336$), IL-10 level ($p = 0.039$, $r = -0.336$), and pain intensity ($p = 0.002$, $r = 0.479$). Finally, the Pearson correlation

analysis for the IL-1β/IL-10 ratio and facet joint histopathology revealed a significant association (p = 0.002, r = 0.490) (Table 4).

Table 3. Spearman Correlation Analysis of IL-1β Level, IL-10 level, and VAS

	p Value	Correlation (r)
IL-1β	0.039	0.336
IL-10	0.039	-0.336
Pain intensity (VAS)	0.002	0.479

Table 4. Pearson Correlation Analysis of IL-1β/IL-10 Ratio and Facet Joint OA Histopathology

	p Value	Correlation (r)
IL-1β /IL-10 Ratio	0.002	0.490

In summary, non-normal distributions were observed for IL-1β, IL-10, and pain intensity, while the IL-1β/IL-10 ratio showed normal distribution. Significant associations were found between IL-1β, IL-10, and pain intensity with facet joint histopathology. Specifically, higher IL-1β levels were positively correlated with histopathological severity, while elevated IL-10 levels and increased pain intensity were negatively correlated. Moreover, the IL-1β/IL-10 ratio demonstrated a positive correlation with facet joint histopathology. These findings provide valuable insights into the interplay of inflammatory markers, pain, and joint pathology in patients undergoing spinal surgery.

DISCUSSION

In this study, 38 patients suffering from degenerative lumbar spinal canal stenosis underwent decompression-stabilization-fusion surgery. Descriptive analysis revealed an average patient age of 58 years, consistent with studies indicating a higher prevalence of lumbar spinal canal stenosis in the 50-60 age range. Studies conducted in Japan showed an increased prevalence with age, reaching 10.8% in the 70–79 age group. The gender distribution in the sample was 52.6% male and 47.4% female, aligning with previous research. Notably, in the 70-79 age range, prevalence was slightly higher in females.[11,12)]

The study investigated biomarkers, revealing an average IL-1β level of 2268.95 pg/ml, indicating high inflammation in the facet joints. This aligns with research indicating elevated pro-inflammatory cytokines, including IL-1β, in degenerative facet joint tissues.[13,14)] The study also observed increased levels of anti-inflammatory cytokines such as IL-10 and IL-13. The average IL-10 level was 1.86 ± 1.68 pg/mL. Elevated IL-10 and IL-4 levels were found in patients with neuropathy without lower back pain, suggesting the analgesic effects of anti-inflammatory cytokines.[15)] Additionally, TNF-alpha and IL-10 levels were significantly higher in the patient group compared to the control group.[16] The mean VAS score was 5.82 ± 0.56, higher than previous studies on lower back pain patients.[17)]

The relationship between IL-1β levels and the histopathological presentation of facet joint osteoarthritis (OA) in lumbar spinal canal stenosis patients was explored. Facet joint degeneration, often termed 'facet joint syndrome,' results from osteoarthritic changes. The study measured IL-1β levels, indicating significantly elevated levels (2268.95 ± 862.80 pg/ml) compared to the cutoff point of 131.0 ± 482.7 pg/ml. IL-1β plays a broad role in facet joint inflammation and degradation, impacting bone cells, synovium, and inflammatory mediators. The study suggested that significant IL-1β levels correlate with facet joint damage, contributing to pain complaints in lumbar spinal canal stenosis patients.

The association between IL-10 levels and the histopathological presentation of facet joint OA was also investigated. IL-10, considered anti-inflammatory, was found to have an average level of 1.86 ± 1.68 pg/mL. This aligns with previous research showing significantly higher IL-10 levels in lumbar canal stenosis patients compared to the control group.[16] Comparisons with another study on low back pain patients demonstrated non-significant differences in IL-10 levels.[18,19]

The study also explored the relationship between pain severity and histopathological presentation of facet joint OA in lumbar spinal canal stenosis patients. The mean VAS score was 5.82 ± 0.56, higher than in previous studies. Significant correlation results (P=0.002) suggested a link between VAS and facet joint OA severity. The study proposed that degeneration-induced inflammation stimulates pain-sensing nerves around the facet joints, contributing to increased pain severity. Pain causes related to facet joints include mechanical pressure, osteoarthritic changes, synovial inflammation, or external injuries.

The investigation delved into the relationship between the IL-1β/IL-10 ratio and the histopathological presentation of facet joint OA in lumbar spinal canal stenosis patients. Limited research exists on the ratio of pro-inflammatory to anti-inflammatory markers in facet joints. The study found a significant association (P=0.002) between the IL-1β/IL-10 ratio and facet joint damage. This implies that a high ratio impacts facet joint damage. These findings align with research indicating that a high IL-6/IL-10 plasma ratio is a significant risk factor for lumbar OA in postmenopausal women with estrogen deficiency.[20,21] Targeting a high pro-inflammatory to anti-inflammatory cytokine ratio could be a therapeutic approach to alleviate complaints and damage in facet joints of lumbar spinal canal stenosis patients. Some studies suggest that individuals with IL-1β deficiency are protected from inflammation-induced osteoarthritis.

CONCLUSION

In conclusion, this study establishes significant correlations between IL-1β levels, IL-10 levels, IL-1β/IL-10 ratio, and the degree of pain with the histopathological features of facet joint osteoarthritis in lumbar spinal canal stenosis patients. These findings highlight the crucial role of inflammatory markers in the complaints and degenerative changes observed in facet joints of Lumbar Spinal Canal Stenosis patients. As a pioneering exploration in this domain, it is recommended that these results serve as a foundation for the development of therapeutic interventions targeting pro-inflammatory cytokines like IL-1β or medications enhancing the role of anti-inflammatory cytokines, such as IL-10. However, further extensive research with larger sample sizes and longer follow-up periods is warranted to refine and validate these findings.

Declaration Of Interest Statement

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CONFLICT OF INTEREST: N/A.

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