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The Relationship between Hypertrophy of the Ligamentum Flavum and Visual Analog Scale and the Ratio of IL-1β/IL-10 Levels in Patients with Lumbar Spinal Canal Stenosis

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ABSTRACT

Introduction: Lumbar Spinal Canal Stenosis (LSCS) or spinal stenosis is a spinal disease characterized by narrowing of the spinal canal due to mechanical compression of the spinal nerve roots. One of the causes of LSCS is Ligamentum Flavum hypertrophy which contributes directly to mechanical compression of nerve fibers or cauda equina. Pain in LSCS can range from mild to severe. An objective assessment of pain that is quite widely used is examination *visual analog scale*.
Methods: This research was carried out at RSUP Prof I.G.N.G. Ngoerah, Denpasar, Bali with research time from January 2023 to January 2024. Clinical and laboratory data were obtained from secondary data from patient medical records. Data analysis in research uses descriptive analysis and inferential analysis.
Results: In this study, a sample of 32 patients was obtained with more males than females with percentages of 56.3% and 43.8%. Based on age, the average is 58 years with the youngest being 40 years and the oldest being 82 years. Based on the analysis carried out, it was found that there was a significant relationship between IL-1β with a value of p = 0.020 and IL-10 with a value of p = 0.030 (p > 0.05) with a positive correlation between IL-1β (0.409) and IL-10 (-0.384). Meanwhile, VAS has a positive correlation strength (0.469) with a p value = 0.007.
Conclusion: The conclusion of this study is that the Visual Analog Scale has a relationship with ligamentum flavum hypertrophy in lumbar spinal canal stenosis and ligamentum flavum hypertrophy has a relationship with the IL-1β/IL-10 ratio in lumbar spinal canal stenosis.

Keywords: LSCS, Ligamentum Flavum Hypertrophy, VAS, IL-1β, IL-10

INTRODUCTION

One of the degenerative spinal diseases that can cause disability is lumbar spinal canal stenosis (LSCS). Lower back pain, pain radiating to the legs, numbness, and intermittent claudication are common symptoms found in elderly people with lumbar disease, one of which is LSCS, where the spinal canal becomes narrower and symptoms arise from nerve compression. The main causes of LSCS are aberrant osteophyte formation within the

facet joints, disc protrusion, and hypertrophy of the ligamentum flavum.

Hypertrophy of the ligamentum flavum is a condition that causes the closure of most of the posterior and lateral parts of the spinal canal; therefore, LF hypertrophy contributes directly to mechanical compression of nerve fibers or the cauda equina, or indirectly causes vascular insufficiency, leading to inadequate blood flow and oxygenation (Moon et al., 2012). the most important thing is that LF hypertrophy is considered a crucial factor and is closely related to the pathogenesis of LSCS (Munns, Joe Y. B. Lee, et al., 2015; Sakai et al., 2017).

Hypertrophy of the ligamentum flavum is associated with the occurrence of LSCS which causes pain ranging from mild in mild cases to severe and makes the patient very disturbed. An objective assessment of pain that is quite widely used is the visual analog scale (VAS) examination. VAS is a psychometric scale of subjective characteristics and is often used to assess pain intensity universally.

Pain assessment with VAS is also supported by several inflammatory markers which are thought to play a role in LF hypertrophy, including Interleukin-1β (IL-1β), Interleukin-10 (IL-10). These markers can be found in LF tissue taken and examined during the decompression-stabilization-fusion procedure (He et al., 2022). Patients with severe LF hypertrophy accompanied by unbearable pain and ineffective conservative treatment must be treated with surgical procedures (Benditz et al., 2019; Sun et al., 2020)

Thus, in this study the author intends to investigate the relationship between several inflammatory markers (IL-1β, IL-10) and the visual analog scale on the degree of canal stenosis narrowing in hypertrophied ligamentum flavum patients with lumbar spinal canal stenosis, which aims to help better understand regarding the inflammatory process that occurs in hypertrophy of the ligamentum flavum as a factor in narrowing canal stenosis.

METHODS

Study Design

This study employed a cross-sectional design analytical observational study. Patient with lumbar canal stenosis was assessed in all study participant. The data obtained from the research is analyzed as follows: Firstly, a descriptive analysis is conducted to provide an overview of the data. Secondly, an inferential analysis is performed, which includes a testing the normality of the data distribution using the Shapiro-Wilk test to determine whether the data follows a normal distribution. Conducting Pearson correlation test if the data is normally distributed, and Spearman correlation test if the data is not normally distributed. These analyses aim to explore relationships and patterns within the data, allowing for a comprehensive understanding of the research findings.The target population comprised all lumbar canal spinal stenosis patients with hypertrophy of ligamentum flavum based on clinical and women aged 65 years and older. The accessible population included women aged older than 40 years and with complete data in medical record of RSUP Prof. dr. I G N G Ngoerah. Consecutive sampling was utilized until the sample size was achieved.

This study included female participants aged older than 40 years and older who had hyperthrophy assessments and had their data stored in the medical records of RSUP Prof dr I G N G Ngoerah Denpasar between January 2023 and January 2024. The research procedure involves initially searching for research samples from

medical records, specifically targeting patients diagnosed with lumbar spinal canal stenosis accompanied by hypertrophy of the ligamentum flavum based on clinical and diagnostic examinations such as MRI. Following patient selection, measurements of pain severity are taken, and laboratory examinations for IL-1β and IL-10 are conducted. Subsequently, samples of the ligamentum flavum are obtained from patients undergoing surgery. These samples undergo histopathological examination using Hematoxylin Eosin staining to evaluate the degree of hypertrophy. Finally, data analysis is performed to derive insights from the collected information.

Data Collection

The data collection method for this study was conducted systematically. Initially, The research was conducted at RSUP Prof. I G.N.G. Ngoerah, Denpasar, Bali. Clinical and laboratory data were obtained from secondary data from patient medical records, with samples of the ligamentum flavum are obtained from patients undergoing surgery, following predefined inclusion and exclusion criteria. Contact details of potential subjects were obtained and used to communicate the research procedures and seek their willingness to participate via telephone or chat applications. Subsequently, anamnesis points were transformed into a structured questionnaire. Upon registration, subjects provided informed consent before undergoing anamnesis and questionnaire completion. Pain severity is assessed through measurements, and laboratory tests are carried out to examine IL-1β and IL-10 levels. Following this, tissue samples of the ligamentum flavum are collected from patients undergoing surgery. These samples are then subjected to histopathological analysis using Hematoxylin Eosin staining to assess the extent of hypertrophy. Finally, the collected data is analyzed to extract meaningful insights.

STATISTICAL ANALYSIS

The data obtained in the study were subjected to two main types of analysis. Firstly, descriptive analysis was conducted to summarize and describe the characteristics of the data. Secondly, inferential analysis was performed, which involved two steps. Initially, the normality of the data distribution was assessed using the Shapiro-Wilk test. If the data were normally distributed, the Pearson Correlation Test was applied to examine correlations between variables. Alternatively, if the data were not normally distributed, the Spearman Test was used instead. These analyses were crucial in understanding the relationships and patterns within the data, providing valuable insights into the research findings.

Furthermore, a Spearman correlation analysis was conducted to examine the relationship between the Histology Degree of Hypertrophy of Ligamentum Flavum and the levels of IL-1β, VAS, and IL-10. Based on the analysis conducted, a significant relationship with p-value ($p > 0.05$). If the study confirms a positive relationship between HLF and IL-10 levels, IL-1β, and VAS the implications could be significant in a clinical context. This understanding may help pave the way for the development of therapies aimed at controlling the inflammatory response, with the hope of reducing symptoms and improving the quality of life of patients.

RESULTS

A. Research Subject Characteristics

In this study, a total of 32 samples were obtained, with demographic characteristics data shown in table 4.1.1. Based on gender, there were more males than females, with a percentage of 56.3% and 43.8% respectively. The average age was 58 years, with the youngest being 40 years old and the oldest being 82.

Table 1 Sample Distribution on Sex

Sex	Total	Percentage
Men	18	56,3 %
Women	14	43,8 %

Table 2 Sample Distribution based on Age

Characteristic	Age
Age Range	40 - 82 tahun
Mean ± SD	57 ± 8.60tahun

B. Inferential Analysis

In this study, a Pearson correlation analysis was conducted to assess the relationship between Histology Degree of Hypertrophy of Ligamentum Flavum and the ratio of IL-1β/IL-10. Based on the conducted test, a significant relationship was found between the histology degree of hypertrophy of the ligamentum flavum and the IL-1β/IL-10 ratio with a p-value of 0.00 ($p < 0.05$), with a weak negative correlation strength (-0.390).

Table 3 Inferential Pearson Analysis for Histology Degree of Hypertrophy of Ligamentum Flavum on IL-1β/IL-10 Rasio

Variable	Correlation	P Value
Ratio IL-1β/IL-10	-0,390	0,00

Table 4 Spearman Correlation Analysis for Histology Degree of Hypertrophy of Ligamentum Flavum with IL-1β, IL-10, VAS Levels

Variable	Correlation	p value
IL-1β	0,409	0.020
IL-10	-0,84	0,030
VAS	0,469	0,007

Furthermore, a Spearman correlation analysis was conducted to examine the relationship between the Histology Degree of Hypertrophy of Ligamentum Flavum and the levels of IL-1β, VAS, and IL-10. Based on the analysis conducted, a significant relationship was found with IL-1β with a p-value of 0.020 and IL-10 with a p-value of 0.030 ($p > 0.05$), with correlation strengths of IL-1β being positive (0.409) and IL-10 being negative (-0.384). Meanwhile, VAS showed a positive correlation strength (0.469) with a p-value of 0.007.

DISCUSSION

A. The relationship between hypertrophy of the ligamentum flavum and the Visual Analog Scale in lumbar spinal canal stenosis.

Lumbar canal stenosis is a common condition in the elderly population, often accompanied by symptoms of lower back and radicular pain. One factor that may play a role in this stenosis is hypertrophy of the ligamentum flavum (HLF), where the elastic ligament between vertebrae undergoes excessive growth. Pain levels in patients can be measured using the Visual Analog Scale (VAS), a subjective measurement tool that provides an indication of how much pain patients are experiencing. The importance of the relationship between HLF and VAS in the context of lumbar canal stenosis lies in understanding the impact of HLF on the intensity of pain perceived by patients. Hypertrophy of the ligamentum flavum can increase pressure on the surrounding nerve structures, which is then reflected in an increase in VAS values. Several empirical studies have been conducted to investigate this relationship, and the results provide insights into its clinical significance.

This study aligns with research conducted by Dawre on 100 patients with hypertrophy

of the ligamentum flavum in lumbar canal stenosis. Significant differences were found in VAS scores according to the degree of hypertrophy of the ligamentum flavum that occurred (p = 0.003). (Dware, 2021) The results of this study are not consistent with the research conducted by Joohyun Kim. In total, 163 patients diagnosed with single-level stenosis (L4-L5) were involved. Patients were divided into 2 groups based on the severity of claudication: >100 m for mild claudication (n = 92) and <100 m for severe claudication (n = 71). The Visual Analog Scale (VAS) was used to measure back and leg pain, but no significant differences were found in VAS scores for back and leg pain (p = 0.598 and p = 0.898). However, in this study, hypertrophy of the ligamentum flavum was found to be a major contributing factor to the severity of claudication (p = 0.105). (Joohyun Kim, 2022) Another study by Haig on 119 patients with lumbar canal stenosis measured hypertrophy of the ligamentum flavum, but no significant differences were found in VAS scores in that study (p = 0.951). (Haig, A.J., 2012)

B. The relationship between hypertrophy of the ligamentum flavum and the level of IL-1β in lumbar spinal canal stenosis.

Lumbar canal stenosis is a condition that can exert pressure on the nerves in that area, leading to symptoms such as pain and discomfort. In this context, hypertrophy of the ligamentum flavum, where the elastic ligament between vertebrae undergoes excessive growth, has been identified as one of the causative factors of this stenosis.

This study explores the relationship between HLF and the level of interleukin-1 beta (IL-1β) in patients with lumbar canal stenosis. IL-1β is a proinflammatory cytokine that can provide insights into the inflammatory response in the body. With the presence of HLF, the initial assumption is that inflammation may be one of the mechanisms involved in the development of stenosis.

Several empirical studies support the association between HLF and increased levels of IL-1β. Elevated IL-1β can be considered an indicator of the inflammatory response related to the extra pressure on the nerves due to hypertrophy of the ligamentum flavum. Therefore, understanding this relationship can help explain the biological aspects of the symptoms experienced by patients with lumbar canal stenosis involving HLF.

The clinical implications of this research involve the potential development of management strategies aimed at controlling the inflammatory response, possibly through anti-inflammatory therapy or other interventions that can reduce symptoms and improve the quality of life of patients. Thus, this study makes a significant contribution to investigating the biological basis of lumbar canal stenosis and provides a foundation for more effective therapeutic approaches. However, as is common in research, it should be noted that there are limitations such as sample size and study design that may affect the generalization of findings.

C. The relationship between hypertrophy of the ligamentum flavum and the level of IL-10 in lumbar spinal canal stenosis.

In this study, special attention is given to IL-10, a type of anti-inflammatory cytokine that plays a role in controlling the inflammatory response. The importance of the relationship between HLF and IL-10 lies in the idea that increased IL-10 levels may be the body's response to the extra pressure generated by HLF. In several empirical

studies, there is strong support for the hypothesis that the correlation between the two can provide a deeper understanding of the biological processes involved in lumbar spinal canal stenosis.

If the study confirms a positive relationship between HLF and IL-10 levels, the implications could be significant in a clinical context. This understanding may help pave the way for the development of therapies aimed at controlling the inflammatory response, with the hope of reducing symptoms and improving the quality of life of patients.

The findings of this study align with research conducted by Efendioglu, which stated that TNF-alpha levels in the patient group were significantly higher statistically compared to the control group ($p=0.004$; $p<0.05$), and IL-10 levels in the patient group were statistically significantly higher compared to the control group ($p=0.017$; $p<0.05$) (Efendioglu, 2020). Conversely, anti-inflammatory markers, including IL-10, have been observed to be significantly lower in subjects experiencing less or no low back pain (LBP). This cytokine is produced by activated macrophages and monocytes and is considered anti-inflammatory because it can inhibit the synthesis of proinflammatory cytokines. In a study by Uçeyler et al., serum IL-10 mRNA levels were found to be higher in painless neuropathy patients. Additionally, Wang et al. found increased IL-10 levels in LBP patients compared to severe cases. IL-10 also correlates negatively with ODI, indicating an analgesic effect of anti-inflammatory cytokines, which may also suggest better treatment outcomes (Khan, 2017).

The expression of IL-10, an anti-inflammatory cytokine, increases during cytokine storms and can facilitate self-protection. Immunosuppression in sepsis is directly related to high IL-10 levels associated with inflammation. Degenerative intervertebral discs and stenosis are also associated with changes in IL-10 levels. Based on research conducted by Duan et al., higher expression levels of IL-6, IL-10, LEP, and TNF-α were found in the tissue of human hypertrophic ligamentum flavum (Duan, 2022).

Thus, this study makes a significant contribution to understanding the relationship between HLF and IL-10 in lumbar spinal canal stenosis. Over time, it is hoped that this knowledge will help lay the groundwork for the development of more sophisticated and effective therapeutic approaches for patients with this condition

D. The relationship between hypertrophy of the ligamentum flavum and the ratio of IL-1β/IL-10 in lumbar spinal canal stenosis.

In the medical field, recent research on the relationship between hypertrophy of the ligamentum flavum (HLF) and the ratio of interleukin-1 beta (IL-1β) to interleukin-10 (IL-10) in lumbar canal stenosis opens a new window in understanding this condition. HLF, characterized by excessive growth of the elastic ligaments between the vertebrae, is often associated with lumbar spinal canal stenosis, which can cause various symptoms such as pain and discomfort. In this study, the focus is on IL-1β as a proinflammatory cytokine and IL-10 as an anti-inflammatory cytokine, with special attention to the IL-1β/IL-10 ratio as an indicator of the balance of the body's inflammatory response. The research hypothesis indicates that in cases of HLF, the IL-1β/IL-10 ratio may increase, indicating a dominance of the proinflammatory response.

The potential findings of this study have significant clinical implications, opening opportunities for a deeper understanding of the inflammatory response in lumbar canal stenosis and leading to the development of therapies that can regulate this balance. However, it is acknowledged that this study has methodological limitations and challenges, such as sample size and study design, which need to be considered in interpreting the results. Therefore, further research is needed to understand in more detail the dynamics of changes in the IL-1β/IL-10 ratio and the potential management strategies that can be implemented in the future. In conclusion, this study makes an important contribution to a deeper understanding of the correlation between HLF and inflammatory response in the context of lumbar canal stenosis.

CONCLUSION

Visual Analog Scale (VAS) exhibits a relationship with hypertrophy of the ligamentum flavum (HLF) in lumbar spinal canal stenosis. Additionally, HLF is associated with the levels of IL-1β in lumbar spinal canal stenosis. Furthermore, HLF correlates with the levels of IL-10 in lumbar spinal canal stenosis. Moreover, HLF is linked to the ratio of IL-1β/IL-10 in lumbar spinal canal stenosis. These findings collectively underscore the multifaceted relationship between HLF and various factors associated with lumbar spinal canal stenosis, providing insights into the pathophysiology of this condition and potentially informing therapeutic interventions.

Declaration by Authors

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