



## COMPARISON OF COMBINED PERINEURAL INJECTION AND ORAL MECOBALAMIN WITH ORAL MECOBALAMIN THERAPY ON SENSORY SYMPTOM IMPROVEMENT IN PATIENTS WITH CARPAL TUNNEL SYNDROME

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### ABSTRACT

Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy, predominantly presenting with sensory symptoms such as numbness and tingling. Conservative therapy with oral mecobalamin is widely used; however, the onset of improvement is often slow. Perineural injection of mecobalamin may provide a faster local effect, but clinical evidence remains limited. This study aimed to evaluate the effectiveness of combined perineural injection and oral mecobalamin compared with oral mecobalamin alone on sensory symptom improvement in CTS patients. This was a comparative interventional study conducted in patients with mild to moderate CTS at Dr. Mohammad Hoesin General Hospital, Palembang. Subjects were divided into two groups: a combination therapy group (perineural injection plus oral mecobalamin) and an oral mecobalamin group. Sensory symptoms were assessed using the Visual Analog Scale (VAS) at baseline, week 2, and week 4. Between-group and within-group comparisons were analyzed using t-tests, while mixed ANOVA was used to evaluate the effects of time and treatment group. Multivariate analysis was performed to identify factors independently associated with sensory symptom improvement. A total of 30 CTS patients were included in this study. There were no significant differences in baseline demographic and clinical characteristics between groups. Mixed ANOVA analysis demonstrated a significant time effect ( $p < 0.001$ ) and a significant time group interaction, indicating a faster pattern of sensory symptom improvement (VAS score reduction) in the combination group. Multivariate analysis showed that combination therapy, sex, and occupation were independently associated with sensory symptom improvement, with occupation being the most dominant factor. The combination of perineural injection and oral mecobalamin is more effective in accelerating and enhancing sensory symptom improvement compared with oral mecobalamin therapy alone in patients with mild to moderate CTS.

Keywords: carpal tunnel syndrome; mecobalamin; perineural injection; sensory symptoms; VAS

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## INTRODUCTION

*Carpal tunnel syndrome* (CTS) is one of the most common forms of entrapment neuropathy encountered in neurological practice. This condition occurs due to increased pressure in the carpal tunnel, which causes dysfunction of the median nerve. The initial clinical manifestations of CTS are generally dominated by sensory complaints such as numbness, tingling, and pain in the thumb, index finger, middle finger, and radial side of the ring finger. In the later stages of the disease, this disorder can progress to a decrease in fine motor function, hand weakness, and thenar muscle atrophy, thereby significantly impacting the patient's daily activities and quality of life (Wahab et al., 2017; Osiak et al., 2022).

Globally, CTS is a health problem with a considerable disease burden. A recent meta-analysis reported that the prevalence of CTS reaches more than 14% in the general population, with wide variations in figures between regions and research methods (Gebrye et al., 2024 2019). These differences are influenced by demographic factors, type of work, and the presence of metabolic

comorbidities. CTS is more common in women and the productive age group, where sensory complaints tend to be more dominant than motor deficits, especially in mild to moderate cases. Complaints of nocturnal paresthesia, a thick feeling in the hands when gripping, and impaired hand dexterity are the most common symptoms and the main reasons patients seek medical help (Dabbagh et al., 2021; Erickson et al., 2019).

The diagnosis of CTS is based on a combination of characteristic medical history, physical examination findings, and supportive tests. Provocation tests such as *Phalen's test*, *Tinel's sign*, and *flick sign* are often used in clinical practice. However, electrodiagnostic tests such as electroneurography and electromyography remain important, especially for confirming the diagnosis, determining the severity, and ruling out possible differential diagnoses such as cervical radiculopathy or other peripheral neuropathies. These tests generally show a slowing of nerve conduction velocity and prolonged distal latency of the median nerve (Winner et al., 2005; Hannaford et al., 2024).

Pathophysiologically, compression of the median nerve leads to segmental demyelination and impaired nerve conduction. Persistent mechanical compression results in disturbances of endoneural microcirculation, disruption of the blood–nerve barrier, and the development of endoneural edema, which further contributes to local ischemia and inflammatory changes. These processes progressively reduce sensory nerve conduction and clinically manifest as paresthesia and pain. With ongoing compression, ischemic injury and endoneural edema may progress to axonal degeneration and neuritis, potentially leading to more permanent sensory deficits in carpal tunnel syndrome (Aboonq, 2015). CTS management is tailored to the severity of the disease. In mild to moderate CTS, conservative therapy is recommended as the first line of treatment. This approach aims to reduce pressure on the median nerve, suppress the inflammatory process, and improve nerve function before permanent damage occurs. Common conservative modalities include wrist splinting, anti-inflammatory drugs, neuropathic drugs, local injections, and neurotrophic vitamin supplementation (Shelke et al., 2023).

Mecobalamin, as an active form of vitamin B12, has long been used in the management of peripheral neuropathy. Pharmacologically, mecobalamin plays a role in supporting axon regeneration and remyelination through increased synthesis of nerve structural proteins and modulation of the inflammatory process. Several studies have shown that mecobalamin administration can improve neuropathic symptoms and nerve conduction parameters, although the results vary depending on the route and duration of administration. A study at Dr. Mohammad Hoesin General Hospital in Palembang compared perineural injections of mecobalamin with 5% dextrose in patients with CTS and found that mecobalamin injections provided significant clinical improvement in patients with mild to moderate CTS (Sugiharto et al., 2024). Another study in Medan reported that oral administration of 500 µg of mecobalamin three times daily for 30 days did not significantly improve nerve conduction velocity and pain in CTS (Sugiharto et al., 2024; Irsyadat et al., 2024).

Oral mecobalamin has a longer clinical effect because it is influenced by absorption and metabolism. In several studies, the results were not significant in improving nerve conduction velocity or sensory symptoms of CTS (Talari, 2017). Conversely, the administration of mecobalamin by injection, particularly perineural injection, allows for higher local concentrations directly around the median nerve, thus providing faster and more significant improvement (Julian et al., 2020). The pharmacological mechanism of injection includes increased bioavailability, direct effects on myelin regeneration, and accelerated improvement of sensory nerve conduction. However, because the effects of injection are limited in duration, combined use with oral administration is expected to provide synergistic effects, with injection providing rapid improvement and oral therapy maintaining long-term systemic effects. To assess the effectiveness of this therapy, measurable clinical and functional parameters are used. *The visual analogue scale*

(VAS) is used to assess the intensity of sensory symptoms such as numbness and tingling before and after therapy, while *the Boston Carpal Tunnel Questionnaire* (BCTQ), which consists of symptom severity and functional status domains, provides a subjective assessment of the patient's quality of life and hand function. Both instruments have been proven to be valid and reliable in evaluating sensory symptoms of CTS and are frequently used in clinical trial studies. Thus, this study specifically compares oral mecobalamin therapy with a combination of perineural injection + oral mecobalamin to evaluate whether the combination can provide faster, more significant, and more lasting improvement in sensory symptoms compared to oral therapy alone.

## METHOD

This study employed a quantitative method with a quasi-experimental design, employing a pre-test and post-test approach with a two-group comparison. Subjects were divided into two groups: one receiving a combination of perineural injection and oral mecobalamin and the other receiving oral mecobalamin alone. The purpose of this study was to determine the effectiveness of the combination of perineural injection and oral mecobalamin compared to oral mecobalamin therapy on improving sensory symptoms in patients with carpal tunnel syndrome. Data collection in this study was conducted prospectively on patients with Carpal Tunnel Syndrome (CTS) undergoing treatment at Dr. Mohammad Hoesin General Hospital, Palembang. Data collection was conducted using several methods, as follows:

1. Data collection on demographic and clinical characteristics  
Demographic and clinical data on CTS patients included age, gender, occupation, affected hand, duration of symptoms, and severity of CTS. This data was obtained through direct interviews with patients, research observation sheets, and patient medical records at Dr. Mohammad Hoesin General Hospital, Palembang.
2. Sensory symptom intensity was measured using a Visual Analog Scale (VAS).  
The intensity of sensory symptoms, including numbness and tingling, was measured using a Visual Analog Scale (VAS). Measurements were taken twice: before therapy (pre-test) and after therapy (post-test) in both treatment groups: the group receiving a combination of perineural injections and oral mecobalamin, and the group receiving oral mecobalamin alone.
3. CTS function and symptoms were assessed using the Boston Carpal Tunnel Questionnaire  
The severity of symptoms and functional impairment due to CTS were assessed using the Boston Carpal Tunnel Questionnaire (BCTQ), which consists of two domains: the Symptom Severity Scale (SSS) and the Functional Status Scale (FSS). The Indonesian version of the BCTQ has been validated and shown to be reliable. Validity testing using Pearson's correlation demonstrated correlation coefficients ranging from  $r = 0.484$  to  $0.781$  (test) and  $0.482$  to  $0.760$  (retest) for the SSS domain, and from  $r = 0.495$  to  $0.825$  (test) and  $0.615$  to  $0.783$  (retest) for the FSS domain. Reliability testing showed good internal consistency, with Cronbach's alpha values of  $0.876$  and  $0.874$  for the SSS domain and  $0.857$  and  $0.854$  for the FSS domain for the test and retest, respectively. In this study, the BCTQ was administered before and after treatment in both groups to objectively and standardize the assessment of changes in hand symptoms and function.
4. Data collection on sensory symptom improvement between groups  
Data on sensory symptom improvement was obtained from the difference in VAS and BCTQ scores before and after therapy in each group. This data was used to compare the level of improvement in sensory symptoms between the group receiving combination therapy with perineural injections and oral mecobalamin and the group receiving oral mecobalamin alone.

The collected data were then analyzed descriptively. Therefore, the hypotheses of this study are:  
H0: There is no significant difference in the improvement of sensory symptoms, such as numbness and tingling, in carpal tunnel syndrome (CTS) patients receiving combination therapy with perineural injections and oral mecobalamin compared to oral mecobalamin therapy. H1: There is a significant difference in the improvement of sensory symptoms, such as numbness and tingling, in carpal tunnel syndrome (CTS) patients receiving combination therapy with perineural injections and oral mecobalamin compared to oral mecobalamin therapy.

## RESULT

### Characteristics of Research Samples

Table 1 shows a comparison of the baseline characteristics of the study subjects based on the type of treatment, namely the combination of perineural injection and oral mecobalamin and the oral mecobalamin therapy groups. The selection of statistical tests for each variable in Table 1 was based on the results of the data normality test. Numerical variables with normal data distribution are presented as the mean  $\pm$  standard deviation and analyzed using the independent t-test. Meanwhile, numeric variables with non-normal distribution are presented as the median and interquartile range and analyzed using the non-parametric Mann Whitney test. For categorical variables, intergroup comparison analysis was performed using the Chi-square test. In general, there were no significant differences in baseline characteristics between the two groups ( $p > 0.05$ ), so the two groups can be considered homogeneous and worthy of comparison.

Table 1.

Comparison of baseline characteristics of research subjects based on treatment

	Oral mecobalamin + perineural mecobalamin injection group	Oral mecobalamin group	Total (%)	p value
Gender				
Female	13 (52.0%)	12 (48.0%)	25 (100%)	0.624 <sup>a</sup>
Male	2 (40.0%)	3 (60.0%)	5 (100%)	
Age (years)	40.93 $\pm$ 6.69	45.53 $\pm$ 7.29		0.083 <sup>b</sup>
BMI	24.03 (20.81-27.59)	23.37 (22.22-26.45)		0.110 <sup>c</sup>
Duration of Symptoms (months)	14.60 $\pm$ 7.09	11.60 $\pm$ 7.33		0.264 <sup>b</sup>
Grade of CTS				
Mild (1-2)	8 (61.5%)	5 (38.5%)	13 (100%)	0.269 <sup>a</sup>
Moderate (3-4)	7 (41.2%)	10 (58.8%)	17 (100%)	
VAS Sensory Symptoms	4.33 $\pm$ 1.44	4.06 $\pm$ 0.96		0.557 <sup>b</sup>
BCTQs	20 (15-25)	18 (16-28)		0.816 <sup>c</sup>
BCTQf	9 (8-10)	9 (7-11)		0.443 <sup>c</sup>
Sensory CTS	52.73 $\pm$ 16.99	43.53 $\pm$ 10.99		0.089 <sup>b</sup>
Occupation (repetitive/non-repetitive)				
Repetitive Movements	14 (51,9%)	13 (48.1%)	27 (100%)	0.543 <sup>a</sup>
Non-repetitive	1 (33,3%)	2 (66.7%)	3 (199%)	
Hand Dominance				
Right	15 (51.7%)	14 (48.3%)	29 (100%)	0.309 <sup>a</sup>
Left	0 (0.0%)	1 (100.0%)	1 (100%)	

Overall, there were no significant differences in baseline demographic and clinical characteristics between the combination therapy group and the oral mecobalamin group (all  $p > 0.05$ ). The majority of subjects in both groups were female, with comparable distributions of age, body mass index, duration of symptoms, CTS severity, and hand dominance. Baseline sensory symptom intensity measured by VAS, as well as symptom severity and functional status assessed by the Boston Carpal Tunnel Questionnaire (BCTQ), were also similar between the two groups. These findings indicate that the two groups were homogeneous at baseline and therefore suitable for comparison in the subsequent analysis of treatment effects.

### Changes in Sensory Symptoms based on VAS Scores

Changes in sensory symptoms in CTS patients in this study were evaluated using a VAS as a subjective measure of the intensity of sensory symptoms. Assessments were conducted repeatedly at several observation time points, namely before intervention (baseline), week 2, and week 4 after therapy administration, both in the combination group of oral mecobalamin and perineural mecobalamin injection and the oral mecobalamin therapy group. This evaluation aimed to assess the pattern of changes in sensory symptoms over time and to compare the effectiveness of both therapy modalities in reducing VAS scores. Statistical analyses were performed to assess the equivalence of baseline conditions between groups, differences in VAS scores between groups at each observation

time, and the interaction between time and type of treatment. The results of the VAS score assessment between treatment groups at each observation time are presented in Table 2.

Table 2.

Assessment of sensory symptoms (VAS) between treatment groups

	Oral mecobalamin + perineural mecobalamin injection group	Oral mecobalamin group	p value	p value time x group
Baseline	4.33 ± 1.44	4.06 ± 0.96	0.557*	
Week 2	1.53 ± 1.55	2.93 ± 1.27	0.012*	0.000**
Week 4	0.93 ± 1.22	1.73 ± 1.22	0.084*	

Table 2 shows a comparison of sensory symptom scores assessed using the VAS between the oral mecobalamin and perineural mecobalamin injection group and the oral mecobalamin therapy group at several observation time points. At baseline, the mean VAS score in the oral mecobalamin and perineural mecobalamin injection group was 4.33±1.44, while in the oral mecobalamin therapy group it was 4.06±0.96. There was no significant difference in baseline VAS scores between the two groups (p=0.557), indicating relatively comparable baseline sensory symptoms. At week 2, the mean VAS scores decreased in both groups, with a greater decrease in the oral mecobalamin and perineural mecobalamin injection group (1.53±1.55) than in the oral mecobalamin therapy group (2.93±1.27). The difference in VAS scores between groups at week 2 was statistically significant (p=0.012). At week 4, the decrease in VAS scores became more pronounced in both groups. The mean VAS score in the combination group of oral mecobalamin and perineural mecobalamin injection was 0.93±1.22, while in the oral mecobalamin therapy group it was 1.73±1.22. The difference in VAS scores between groups at week 4 was statistically significant (p=0.084). Overall, the results of the mixed ANOVA analysis showed a significant effect of time on VAS scores (p<0.001), indicating improvement in sensory symptoms over time in both groups. Furthermore, there was a significant interaction between time and group (p<0.05), indicating that the pattern of decline in VAS scores in the combination group of oral mecobalamin and perineural mecobalamin injection was faster than in the oral mecobalamin therapy group alone.

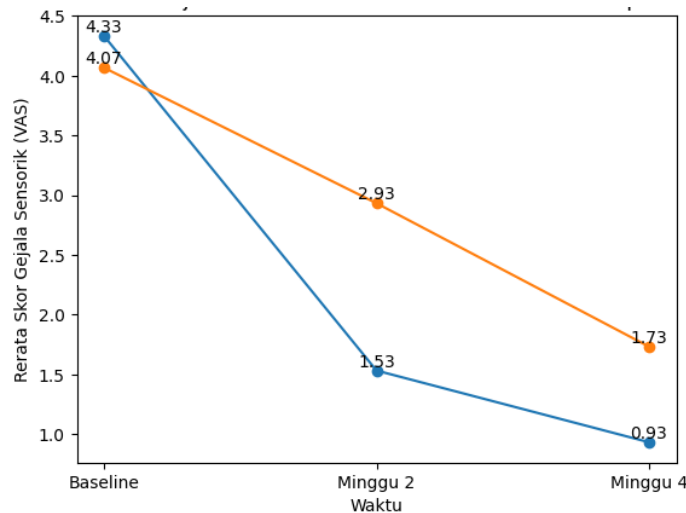


Figure 1. Graph of sensory symptom improvement based on time and intervention group

Based on the sensory symptom improvement graph, it can be seen that both intervention groups experienced a decrease in the average VAS score over time, both from baseline to week 2 and from week 2 to week 4. However, the pattern of VAS score decline in the combination group of perineural injection and oral mecobalamin appeared sharper than the oral mecobalamin therapy group alone. This pattern illustrates that the combination group of perineural injection and oral mecobalamin experienced a faster and greater improvement in sensory symptoms than the oral mecobalamin therapy group alone during the observation period.

Table 3. Changes in sensory symptoms ( $\Delta$  VAS) over time

	Oral mecobalamin + perineural mecobalamin injection group	Oral mecobalamin group	p value*
$\Delta$ 0-2 weeks	2.80 $\pm$ 0.41	1.13 $\pm$ 0.74	0.000
$\Delta$ 2-4 weeks	0.60 $\pm$ 0.51	1.20 $\pm$ 0.68	0.010
$\Delta$ 0-4 weeks	3.40 $\pm$ 0.51	2.47 $\pm$ 1.13	0.007

Table 3 shows a comparison of changes in sensory symptom scores as measured by the visual analog scale ( $\Delta$ VAS) at several observation time intervals between the combination group of oral mecobalamin with perineural mecobalamin injection and the oral mecobalamin therapy group. At the 0–2 week interval, the mean decrease in VAS scores in the combination group of oral mecobalamin and perineural mecobalamin injection was 2.80 $\pm$ 0.41, while the decrease in VAS scores was 1.13 $\pm$ 0.74 in the oral mecobalamin therapy group. The difference in VAS score reduction between the two groups during this period was statistically significant (p=0.000), indicating a more rapid improvement in sensory symptoms in the combination group. At the 2–4 week interval, the combination group of oral mecobalamin and perineural mecobalamin injection continued to show a greater decrease in VAS scores, at 0.60 $\pm$ 0.51, compared to the oral mecobalamin therapy group, at 1.20 $\pm$ 0.68. The difference in VAS score change during this period was also statistically significant (p=0.010). Cumulatively, over the 0–4 week interval, the mean decrease in VAS scores in the combination group of oral mecobalamin and perineural mecobalamin injection reached 3.40 $\pm$ 0.51, while in the oral mecobalamin therapy group it was 2.47 $\pm$ 1.13. The difference in total decrease in VAS scores between the two groups was statistically significant (p=0.007). These results indicate that the combination of oral mecobalamin with perineural mecobalamin injection provided greater and faster improvement in sensory symptoms than oral mecobalamin therapy alone during the four-week observation period.

### Changes in BCTQ Scores in the Symptom Severity and Functional Status Domains

In addition to assessing sensory symptoms using a VAS, this study also evaluated the impact of the intervention on symptom severity and functional status in carpal tunnel syndrome (CTS) patients using the Boston Carpal Tunnel Questionnaire (BCTQ). This instrument consists of two main domains: the symptom severity scale (SSS), which assesses subjective symptom severity, and the functional status scale (FSS), which describes limitations in hand function during daily activities. BCTQ scores were assessed at two observation points: before the intervention (baseline) and at the end of the fourth week, in both the oral mecobalamin and perineural mecobalamin injection combination group and the oral mecobalamin therapy group. This evaluation aimed to assess changes in BCTQ scores within each group and to compare the magnitude of improvement between treatment groups. Statistical analysis was chosen based on the non-normal distribution of the data, therefore non-parametric tests were used to assess intra-group changes and inter-group differences.

Table 4.  
Changes in BCTQ symptom severity scale scores

	Oral mecobalamin + perineural mecobalamin injection group		Oral mecobalamin group		p value <sup>a</sup>
	median (min-max)	mean $\pm$ SD	median (min-max)	mean $\pm$ SD	
Baseline Evaluation	20 (15-25)	19,33 $\pm$ 2,72	18 (16-28)	19,40 $\pm$ 3,46	0.816
Baseline Evaluation	11 (11-20)	13,27 $\pm$ 3,15	17 (11-22)	16,53 $\pm$ 3,54	0.024
p value <sup>b</sup>		0.001		0.005	

Table 4 shows changes in BCTQ symptom severity scale scores in the two intervention groups: the oral mecobalamin + perineural mecobalamin injection group and the oral mecobalamin group, assessed at baseline and the week 4 evaluation. In addition to describing the changes in scores within each group, this table also presents comparisons between groups at each measurement time. At baseline, the median BCTQ symptom severity scale score in the combination group was 20 (min–max 15–25), while in the oral mecobalamin group it was 18 (16–28). Analysis using the Mann–Whitney test revealed no statistically significant difference between the two groups at baseline (p=0.816), indicating that the severity of sensory symptoms at baseline was relatively

comparable. At the week 4 evaluation, the median BCTQ symptom severity scale score in the combination group decreased to 11 (11–20), while in the oral mecobalamin group it was 17 (11–22). The Mann–Whitney test results at the time of evaluation showed a statistically significant difference between the two groups ( $p = 0.024$ ), with lower scores in the combination group.

Analysis of score changes within each group using the Wilcoxon test showed that both groups experienced a significant decrease in BCTQ symptom severity scale scores. In the oral mecobalamin + perineural mecobalamin injection group, the decrease in scores from baseline to the week 4 evaluation was statistically significant ( $p = 0.001$ ). Similarly, in the oral mecobalamin group, the decrease in scores from baseline to the week 4 evaluation was also significant ( $p = 0.005$ ). These findings indicate that both interventions were effective in improving subjective sensory symptoms after four weeks of therapy, but the improvement in the combination group was greater than that in oral mecobalamin alone, as demonstrated by the significant difference between groups at the final evaluation.

Table 5.  
Changes in BCTQ functional status scale scores

	Oral mecobalamin + perineural mecobalamin injection group		Oral mecobalamin group		p value <sup>a</sup>
	median (min-max)	mean ± SD	Median (min-max)	mean ± SD	
Baseline Evaluation	9 (8-10)	9,07±0,79	9 (7-11)	8,80±1,08	0.443
Baseline Evaluation	8 (8-9)	8,33±0,49	8 (5-11)	8,33±1,49	0.817
p value <sup>b</sup>	0.001		0.020		

Table 5 shows the changes in BCTQ functional status scale scores in the two intervention groups: the oral mecobalamin + perineural mecobalamin injection group and the oral mecobalamin group, assessed at baseline and at the 4-week evaluation. This table illustrates the changes in scores within each group and the comparison between groups at each measurement time. At baseline, the median BCTQ functional status scale score in the combination group was 9 (min–max 8–10), while in the oral mecobalamin group it was 9 (7–11). Analysis using the Mann–Whitney test showed no statistically significant difference between the two groups at baseline ( $p=0.443$ ), indicating that hand functional status at baseline was relatively comparable. At the 4-week evaluation, the median BCTQ functional status scale score in the combination group decreased to 8 (8–9), while in the oral mecobalamin group it was 8 (5–11). The Mann–Whitney test results showed no statistically significant difference between the two groups at the evaluation time ( $p=0.817$ ). Analysis of score changes in each group using the Wilcoxon test showed that both groups experienced a statistically significant decrease in BCTQ functional status scale scores. In the oral mecobalamin + perineural mecobalamin injection group, the decrease in scores from baseline to the 4-week evaluation was significant ( $p = 0.001$ ). Similarly, in the oral mecobalamin group, the decrease in scores from baseline to the 4-week evaluation was also significant ( $p = 0.020$ ). These findings indicate that both interventions were effective in improving hand functional status after four weeks of therapy. However, no significant difference was found between the two groups at the final evaluation, indicating that the degree of improvement in hand function achieved was relatively comparable between combination therapy and oral mecobalamin therapy alone during the observation period of this study.

Table 6.  
Comparison of changes in BCTQ scores

	Oral mecobalamin + perineural mecobalamin injection group		Oral mecobalamin group		p value
	median (min-max)	mean ± SD	median (min-max)	mean ± SD	
Δ skor sBCTQ	5 (3-9)	6,07±2,31	3 (0-7)	2,87±2,67	0.008
Δ skor fBCTQ	1 (0-1)	0,73±0,45	0 (0-2)	0,47±0,64	0.130

Table 6 shows a comparison of changes in BCTQ scores between the combination group of oral mecobalamin + perineural mecobalamin injection and the oral mecobalamin therapy group during the observation period. The median change in BCTQ symptom severity scale ( $\Delta$ sBCTQ) scores in the combination group of oral mecobalamin and perineural mecobalamin injection was 5 (3-9), while in the oral mecobalamin therapy group it was 3 (0-7). The Mann-Whitney test showed that the difference in sBCTQ score changes between the two groups was statistically significant ( $p=0.008$ ), indicating greater subjective symptom improvement in the combination group. Meanwhile, the median change in BCTQ functional status scale ( $\Delta$ fBCTQ) scores in the combination group of oral mecobalamin and perineural mecobalamin injection was 1 (0-1), while in the oral mecobalamin therapy group it was 0 (0-2). The difference in median changes in fBCTQ scores between the two groups was not statistically significant ( $p=0.130$ ). These results indicate that the combination of oral mecobalamin with perineural mecobalamin injection provides more significant improvement in subjective sensory symptoms than oral mecobalamin therapy alone, but improvement in hand function as measured by the fBCTQ has not shown significant differences between the two groups during the observation period.

### Multivariate Analysis of Factors Affecting Changes in VAS Scores of Sensory Symptoms

To assess the independent effect of the intervention and confounding factors on changes in the VAS score for sensory symptoms ( $\Delta$ VAS), a multivariate analysis using linear regression was performed. This analysis aimed to identify variables that significantly contributed to the magnitude of sensory symptom improvement after the intervention, taking into account various demographic and clinical characteristics of the study subjects. Variables included in the model included the type of intervention, age, gender, body mass index (BMI), duration of symptoms, CTS severity, sensory KHS score, baseline VAS score, type of occupation, and hand dominance. Variable selection was based on their clinical relevance and potential role as confounding factors on the outcome of changes in VAS scores. The results of the multivariate analysis using multiple linear regression with the backward method on changes in the VAS score for sensory symptoms are presented in Table 13. The table contains the regression coefficient ( $\beta$ ), 95% confidence interval (95% CI), and the level of statistical significance of each variable included in the final model.

Table 7.

Multivariate analysis of changes in VAS scores ( $\Delta$ VAS) of sensory symptoms							
Intervention Variables	B	$\beta$	t	p	partial r	part r	95% CI
Gender	-0,683	-0,355	-2,858	0,008	-0,498	-0,331	-1,176 s/d - 0,191
Occupation	-1,142	-0,442	-3,754	0,001	-0,598	-0,432	-1,772 s/d - 0,512
Intervention Variables	-1,869	-0,484	-3,955	0,001	-0,620	-0,457	-2,842 s/d - 0,896

Table 7 presents the results of a multivariate linear regression analysis of changes in VAS scores ( $\Delta$ VAS) for sensory symptoms in carpal tunnel syndrome patients. This analysis was conducted to assess the independent effects of intervention, gender, and occupation on improvement in sensory symptoms after controlling for other confounding variables. Variables included in the model were those with clinical relevance and/or demonstrated a significant relationship in the previous bivariate analysis. Based on the table, all three variables intervention, gender, and occupation showed a statistically significant relationship with changes in VAS scores ( $p<0.05$ ). The negative regression coefficient (B) values for all three variables indicate that each factor is associated with a decrease in VAS scores, reflecting improvement in sensory symptoms. The standardized beta ( $\beta$ ) value indicates that occupation had the greatest relative influence on improvement in sensory symptoms, followed by gender and intervention. Furthermore, the partial correlation (partial r) and semi-partial correlation (part r) values indicate the strength of each variable's relationship with changes in VAS scores after controlling for other variables in the model. The occupation variable had the highest partial r and partial r values, indicating that this factor was the most dominant determinant independently associated with improvement in sensory symptoms. Meanwhile, gender and

intervention variables also showed significant contributions, but with lower strengths of association than occupation. The 95% confidence intervals (95% CIs) that did not cross zero for all three variables confirmed that the observed effects were consistent and statistically significant. Overall, this table confirms that improvement in sensory symptoms in CTS patients is influenced not only by the intervention but also by individual factors such as gender and occupational characteristics. The results of multivariate analysis using multiple linear regression showed that intervention, gender, and occupation were significantly associated with changes in VAS scores for sensory symptoms. Based on standardized beta values and partial correlation, occupational variables had the most dominant influence on sensory symptom improvement ( $\beta = -0.484$ ; partial  $r = -0.620$ ;  $p = 0.001$ ), followed by gender ( $\beta = -0.442$ ; partial  $r = -0.598$ ;  $p = 0.001$ ) and intervention ( $\beta = -0.355$ ; partial  $r = -0.498$ ;  $p = 0.008$ ). Meanwhile, age, body mass index, symptom duration, CTS severity, baseline VAS score, and hand dominance did not show a statistically significant effect on VAS score changes ( $p > 0.05$ ). These findings indicate that after simultaneous control in the multivariate model, these variables do not contribute independently to the magnitude of sensory symptom improvement in CTS patients.

## **DISCUSSION**

The results showed that the baseline characteristics of the study subjects, including age, gender, duration of symptoms, type of employment, body mass index, hand dominance, and initial CTS severity, did not differ significantly between the oral mecobalamin therapy group and the combination perineural injection and oral mecobalamin group. Therefore, both groups can be considered homogeneous and worthy of comparison. Homogeneity of baseline characteristics is an important aspect in intervention studies because it minimizes the influence of confounding factors on clinical outcomes. Theoretically, advanced age, female gender, obesity, and occupations involving repetitive motions are risk factors that play a role in the pathogenesis of CTS and can influence therapeutic response. The lack of significant differences in these factors indicates that the differences in clinical outcomes obtained are primarily due to the intervention provided. This finding is consistent with previous studies that stated that mild to moderate CTS with predominantly sensory complaints is most often found in the productive age population and women, and is the group most responsive to conservative therapy (Erickson et al., 2019; Del Barrio et al., 2018; Hernández et al., 2021).

Based on the study results, both treatment groups showed a decrease in visual analog scale (VAS) scores for sensory symptoms after the intervention, both in weeks 2 and 4, indicating an improvement in numbness, tingling, and neuropathic pain in carpal tunnel syndrome (CTS) patients. However, the group receiving the combination of perineural injection and oral mecobalamin showed a greater, faster, and more consistent reduction in VAS scores than the oral mecobalamin-only group. Mixed ANOVA results revealed a significant effect of time ( $p < 0.001$ ) and a significant interaction between time and group ( $p < 0.05$ ), indicating that the pattern of sensory symptom improvement differed between groups over time, with the combination of perineural injection and oral mecobalamin being superior.

At baseline, the VAS scores of both groups were relatively comparable and did not differ significantly, indicating that the severity of sensory symptoms at the beginning of the study was at a similar level. This is important because it confirms that subsequent differences in improvement are more likely due to the intervention effect, rather than differences in baseline conditions. At week 2, the combination group showed a statistically significant and greater reduction in VAS scores compared to the oral-only group (mean $\pm$ SD  $\Delta$ VAS =  $2.80 \pm 0.41$ ;  $p = 0.000$ ). This trend continued until week 4, where the combination group's VAS scores remained lower. Furthermore, analysis of the change in scores ( $\Delta$ VAS) showed that the cumulative reduction from 0–4 weeks was significantly greater in the combination group (mean $\pm$ SD  $\Delta$ VAS =  $3.40 \pm 0.51$ ;  $p = 0.007$ ), confirming that the combination group achieved a greater clinical benefit over the 4-week observation period.

Pathophysiologically, the symptoms of numbness and tingling in CTS are primarily caused by impaired endoneural microcirculation, perineural edema, and segmental demyelination of the median nerve sensory fibers. This condition leads to sensory nerve hyperexcitability and neuropathic pain. Mecobalamin plays a role in improving these conditions by increasing remyelination, Schwann cell differentiation, and modulating inflammatory mediators such as TNF- $\alpha$  and IL-6. Perineural administration of mecobalamin allows for higher local concentrations around the median nerve, thereby accelerating repair of the nerve microenvironment and reducing pain sensitization. This explains the faster and more significant improvement in VAS scores in the combination group compared to oral therapy alone. The combination group used perineural injection, which allows for higher local concentrations of mecobalamin around the median nerve, thereby accelerating repair of the nerve microenvironment and reducing peripheral sensitization. Although published evidence from large clinical trials specifically evaluating perineural mecobalamin for CTS is limited, the perineural approach using hydrodissection alone has been shown to improve CTS symptoms in studies with other injectable agents. Furthermore, perineural mecobalamin administration in other peripheral neuropathies has been reported to be associated with clinical improvement. The findings of this study can be understood as a combination of the mechano-biological effects of the perineural approach in improving the neural microenvironment, plus the potential neurotrophic effects of mecobalamin on remyelination and sensory fiber regeneration. These findings are consistent with previous studies showing that perineural mecobalamin injection in peripheral neuropathies provides significant reductions in neuropathic pain within a relatively short time, as well as meta-analyses reporting the effectiveness of mecobalamin in reducing neuropathic pain with a favorable safety profile (Julian et al., 2020; Sawangjit et al., 2020; Ma et al., 2022).

The results of this study showed that BCTQ scores, both in the symptom severity and functional status domains, improved in both groups. However, the group with the combination of perineural injection and oral mecobalamin showed greater improvement, particularly in the symptom severity domain. The BCTQ is a widely validated instrument and is considered the standard in evaluating CTS clinical outcomes because it captures two key aspects of the disease: subjective symptom severity (SSS) and functional impact on daily activities (FSS). The SSS domain assesses the intensity and frequency of nocturnal paresthesias, pain on gripping, weakness, and numbness, while the FSS domain describes functional limitations in activities such as writing, holding small objects, opening bottles, or carrying items. Therefore, improvements in BCTQ scores reflect not only changes in symptoms but also direct implications for patients' quality of life and independence. In this study, the median BCTQ SSS score in the combination group decreased significantly from baseline to week 4, and this decrease was greater than in the oral-only group. Clinically, this indicates that patients in the combination group experienced faster and more pronounced improvement in paresthesias, pain reduction, and reduced sleep disturbances due to sensory complaints. This pattern aligns with the characteristics of CTS, where sensory symptoms are the initial and dominant manifestation due to impaired endoneural microcirculation, perineural edema, and segmental demyelination of the median nerve. The superior improvement in SSS in the combination group can be explained by several mechanisms.

Chronic compression of the carpal tunnel causes increased intracanal pressure, which impairs blood flow to the vasa nervorum, leading to local hypoxia, edema, and perineural inflammation. This condition increases the excitability of A $\beta$  and C sensory fibers, which trigger neuropathic pain and paresthesia. Mecobalamin (methylcobalamin) has neurotrophic effects by increasing myelin synthesis, stimulating Schwann cell differentiation, and supporting axon regeneration. Furthermore, mecobalamin has been reported to reduce inflammatory mediators and oxidative stress, thus helping to improve the neural microenvironment. Perineural administration of mecobalamin offers the added advantage of achieving higher local concentrations around the median nerve. Thus, neuroregenerative and anti-inflammatory effects may occur more rapidly and be more focused on

the lesion site. This explains why subjective symptom improvement, as assessed by SSS, was more pronounced in the combination group compared to oral therapy alone, which depends on systemic absorption and tissue distribution. This concept aligns with the principle that in compression neuropathy, local therapy may have a more rapid effect in improving the neural microenvironment. The findings of this study are consistent with previous research at Dr. Mohammad Hoesin General Hospital, Palembang, which showed that perineural mecobalamin injection provided significant clinical improvement in patients with mild-moderate CTS (Sugiharto et al., 2024).

The advantage of the combination approach in this study lies in the synergistic effect between perineural injection and oral mecobalamin therapy. Perineural injection provides a rapid effect by increasing local concentration and improving the median nerve microenvironment, while oral therapy plays a role in maintaining medium- to long-term systemic neuroprotective effects. This approach aligns with the concept of multimodal conservative therapy for mild to moderate CTS recommended by the American Academy of Neurology, where combination therapy aims to address inflammation, improve nerve conduction, and prevent the progression of axonal damage. Therefore, the results of this study strengthen the rationale for using perineural mecobalamin injection as an adjunct to standard therapy in CTS patients with predominantly sensory symptoms (Sugiharto et al., 2024; Talari, 2017).

Multivariate linear regression analysis showed that intervention, gender, and occupation were factors independently associated with improvement in sensory symptoms in carpal tunnel syndrome patients ( $p < 0.005$ ). This finding confirms that the improvement in sensory symptoms is not solely influenced by the subject's baseline characteristics but is a direct effect of the combined intervention and is influenced by individual biological and biomechanical factors. The occupational variable showed the most dominant influence on changes in VAS scores, as indicated by the highest standardized beta value ( $\beta = -0.484$ ) and the largest partial correlation ( $r = -0.620$ ) and part correlation ( $r = -0.457$ ). This indicates that occupational characteristics, particularly those involving repetitive hand activities, repeated wrist flexion-extension movements, and exposure to chronic mechanical stress, play a significant role in determining the extent of sensory symptom improvement. In individuals with occupations requiring intensive hand use, the median nerve compression process tends to be more severe and persistent, so the response to therapy may differ compared to individuals with lighter biomechanical stress. This finding is in line with the pathophysiological concept of CTS that repetitive mechanical stress can exacerbate endoneural edema, microcirculatory disorders, and segmental demyelination, thereby affecting the degree and speed of sensory function recovery (Malik et al., 2023; Aboonq, 2015).

Gender showed a significant independent association with improvement in sensory symptoms, with a standardized beta value of  $-0.442$ , a partial correlation of  $-0.598$ , and a partial correlation of  $-0.432$  ( $p = 0.001$ ). Women are known to have a higher prevalence of CTS and tend to report more severe pain intensity and paresthesia. This is thought to be related to hormonal factors, differences in pain threshold, the relatively narrower size of the carpal tunnel, and tissue sensitivity to pressure changes. Several studies have shown that hormonal fluctuations, particularly estrogen, can affect fluid retention and connective tissue elasticity, which in turn can increase intracanal pressure. Thus, the differences in treatment response based on gender found in this study are biologically understandable and support the results of the multivariate analysis.

The combined intervention of perineural injection and oral mecobalamin also demonstrated a significant independent association with improvement in sensory symptoms, with a standardized beta value of  $-0.355$ , a partial correlation of  $-0.498$ , and a partial correlation of  $-0.331$  ( $p = 0.008$ ). The negative regression coefficient indicates that the combination therapy is associated with a greater reduction in VAS scores than oral therapy alone. Pharmacologically, perineural injection allows for higher concentrations of mecobalamin around the median nerve, resulting in a more rapid

local effect in repairing myelin function, suppressing inflammation, and improving sensory nerve conduction. Meanwhile, oral administration plays a role in maintaining long-term systemic effects. The combination of these two routes theoretically provides a synergistic effect, with injection contributing to the initial phase of repair, while oral therapy maintains ongoing nerve regeneration.

The lack of a significant effect of age, body mass index, symptom duration, CTS severity, baseline VAS score, and hand dominance in the multivariate model indicates that, after simultaneous control, these factors did not independently contribute to the extent of sensory symptom improvement. This indicates that the response to therapy in this study was more determined by the type of intervention administered and certain individual characteristics such as gender and occupation, rather than by other demographic or clinical factors. This finding is important because it confirms that the observed effect of combination therapy is not biased by differences in baseline subject characteristics, but rather represents a real intervention effect. Overall, the results of the multivariate analysis in this study support the hypothesis that the combination of perineural injection and oral mecobalamin provides greater clinical benefit in accelerating and enhancing sensory symptom improvement in patients with mild to moderate CTS. Furthermore, the role of occupation and gender as factors influencing therapy response needs to be considered in clinical practice, particularly in patient education, therapy planning, and relapse prevention efforts.

Several limitations of this study should be considered in interpreting the results. The limited follow-up duration of only a few weeks prevented a comprehensive evaluation of the long-term effects of therapy. Furthermore, this study did not assess objective changes in electrophysiological parameters post-intervention that could provide a structural correlation to clinical improvement. Nevertheless, the randomized controlled trial design and homogeneity of baseline characteristics provide sufficient methodological strength to conclude the effectiveness of combination therapy in improving sensory symptoms in mild-moderate CTS. Clinically, the results of this study suggest that the combination of perineural injection and oral mecobalamin therapy may be an effective and rational conservative treatment option in patients with mild-moderate CTS with predominantly sensory symptoms. This approach has the potential to provide more rapid and meaningful symptom improvement while maintaining clinical outcomes through continued oral therapy (Chang, 2020; Sugiharto et al., 2024).

In this study, no serious adverse events were observed in either the oral mecobalamin therapy group or the combination group of perineural injections and oral mecobalamin during the study period. Reported adverse events were mild, transient, and did not require discontinuation of therapy, allowing all subjects to complete the intervention according to the study protocol. In the combination group, the most common complaints were mild pain or discomfort at the injection site, which was transient and resolved spontaneously within a short period of time. There were no signs of serious complications such as local infection, bleeding, allergic reactions, or new neurological deficits after injection. These findings indicate that perineural mecobalamin injection has a good safety profile when performed with proper technique (Chiu et al., 2011; Chen et al., 2023).

Mecobalamin is known as a neurotropic agent with an excellent safety profile, both in oral and injectable forms. Unlike corticosteroid injections, which can potentially cause local side effects such as tissue atrophy, hypopigmentation, or increased local pressure in the carpal tunnel, mecobalamin has no catabolic effects on soft tissue and does not exacerbate median nerve compression. This is one of the advantages of mecobalamin as an adjunct therapy for mild to moderate CTS. Several previous studies support these safety findings, noting that the use of methylcobalamin for peripheral neuropathy was not associated with an increased incidence of serious adverse events compared with placebo. Reported side effects were generally mild, such as local pain after injection or mild gastrointestinal complaints with oral administration, and were reversible (Sawangjit et al., 2020; Amin et al., 2024). Thus, the results of this study strengthen the

evidence that the combination of perineural injection and oral mecobalamin therapy is not only effective in improving sensory symptoms of CTS but also has a good safety profile. Considering the clinical efficacy, pathophysiological rationale, and good safety profile, the combination of perineural injection and oral mecobalamin therapy is worthy of consideration as an initial conservative treatment strategy for mild-moderate CTS with predominantly sensory symptoms, especially in productive-age patients.

## CONCLUSION

The demographic and clinical characteristics of carpal tunnel syndrome patients in this study showed that CTS sufferers were predominantly women of productive age and overweight. Clinically, the duration of symptoms was relatively similar between the two groups (14.60±7.09 months vs. 11.60±7.33 months). The severity of CTS was mild to moderate, with an equal distribution between the groups. Most patients had jobs involving repetitive movements (51.9% vs. 48.1%) and were right-handed (51.7% vs. 48.3%). Based on the assessment of sensory symptom intensity using a visual analog scale (VAS), the pattern of sensory symptom reduction differed between the groups, with faster and greater improvement in the group with the combination of perineural injection and oral mecobalamin compared to oral mecobalamin therapy alone ( $p=0.000$ ). At week 2, the combination group showed a greater reduction in VAS scores than the oral group (1.53±1.55 vs. 2.93±1.27), and this difference was statistically significant ( $p=0.012$ ). At week 4, VAS scores remained lower in the combination group than in the oral group (0.93±1.22 vs. 1.73±1.22), although the difference between groups was no longer statistically significant ( $p=0.084$ ). Based on the Boston Carpal Tunnel Questionnaire (BCTQ) symptom severity and functional status scores, significant improvements were observed in both groups after 4 weeks of therapy. In the combination group with perineural injection and oral mecobalamin, symptom severity scores improved from 19.33 to 13.27 ( $p=0.000$ ) and functional status scores improved from 9.07 to 8.33 ( $p=0.000$ ). In the oral mecobalamin group, there was also an improvement in symptom severity scores from 19.40 to 16.53 ( $p=0.001$ ) and functional status from 8.80 to 8.33 ( $p=0.014$ ). Sensory symptom improvement in CTS patients receiving the combination of perineural injection and oral mecobalamin was significantly better than in patients receiving oral mecobalamin alone. In addition to the combination intervention, gender and occupation were also significantly associated with improvement in sensory symptoms, with occupation being the most dominant factor.

## REFERENCES

- Aboonq, M. S. (2015). Pathophysiology of carpal tunnel syndrome. *Neurosciences Journal*, 20(1), 04-09.
- Amin, R., Alam, F., Kemisetti, D., Sarkar, D., & Dey, B. K. (2024). Carpal Tunnel Syndrome Management by Nutraceuticals. In *Nutraceuticals and Bone Health* (pp. 205-219). Apple Academic Press.
- Chang, R. (2020). *Conservative Treatment Vs. Corticosteroid Injection with or Without Other Conservative Treatments for Carpal Tunnel Syndrome*. California State University, Fresno.
- Chen, C. H., Huang, H. Y., Huang, A. P. H., Jaw, F. S., Chen, M. C., Lin, C. W., & Wang, S. P. (2023). Ultrasound-guided perineural vitamin B12 injection for brachial plexus injury: a preliminary study. *Cell Transplantation*, 32, 09636897231167213.
- Chiu, C. K., Low, T. H., Tey, Y. S., Singh, V. A., & Shong, H. K. (2011). The efficacy and safety of intramuscular injections of methylcobalamin in patients with chronic nonspecific low back pain: a randomised controlled trial. *Singapore medical journal*, 52(12), 868.
- Dabbagh, A., MacDermid, J. C., Yong, J., Packham, T. L., Macedo, L. G., & Ghodrati, M. (2021). Diagnostic accuracy of sensory and motor tests for the diagnosis of carpal tunnel syndrome: a systematic review. *BMC Musculoskeletal Disorders*, 22(1), 337.
- Del Barrio, S. J., Gracia, E. B., García, C. H., de Miguel, E. E., Moreno, J. T., Marco, S. R., & Laita, L. C. (2018). Conservative treatment in patients with mild to moderate carpal tunnel syndrome: A systematic review. *Neurología (English Edition)*, 33(9), 590-601.

- Erickson, M., Lawrence, M., Jansen, C. W. S., Coker, D., Amadio, P., Cleary, C., ... & Yung, E. (2019). Hand pain and sensory deficits: carpal tunnel syndrome: clinical practice guidelines linked to the international classification of functioning, disability and health from the academy of hand and upper extremity physical therapy and the academy of orthopaedic physical therapy of the American physical therapy association. *Journal of Orthopaedic & Sports Physical Therapy*, 49(5), CPG1-CPG85.
- Gebrye, T., Jeans, E., Yeowell, G., Mbada, C., & Fatoye, F. (2024). Global and regional prevalence of carpal tunnel syndrome: A meta-analysis based on a systematic review. *Musculoskeletal Care*, 22(4), e70024.
- Hannaford, A., Paling, E., Silsby, M., Vincenten, S., van Alfen, N., & Simon, N. G. (2024). Electrodiagnostic studies and new diagnostic modalities for evaluation of peripheral nerve disorders. *Muscle & Nerve*, 69(6), 653-669.
- Hernández-Secorún, M., Montaña-Cortés, R., Hidalgo-García, C., Rodríguez-Sanz, J., Corral-de-Toro, J., Monti-Ballano, S., ... & Lucha-López, M. O. (2021). Effectiveness of conservative treatment according to severity and systemic disease in carpal tunnel syndrome: a systematic review. *International journal of environmental research and public health*, 18(5), 2365.
- Irsyadat, A. M., Aulina, S., Goysal, Y., Zainuddin, A. A., Lotisna, M., & Amran, M. Y. (2024). Comparison of Giving Mecobalamin Supplements to Improve the Severity of Painful Diabetic Neuropathy. *Jurnal Ilmiah Kesehatan (JIKA)*, 6(3), 452-462.
- Julian, T., Syeed, R., Glasgow, N., Angelopoulou, E., & Zis, P. (2020). B12 as a treatment for peripheral neuropathic pain: a systematic review. *Nutrients*, 12(8), 2221.
- Lundborg, G., & Dahlin, L. B. (1992). The pathophysiology of nerve compression. *Hand clinics*, 8(2), 215-227.
- Ma, Y., Chen, J., Huang, X., & Liu, Y. (2022). The efficacy and safety of mecobalamin combined with Chinese medicine injections in the treatment of diabetic peripheral neuropathy: a systematic review and Bayesian network meta-analysis of randomized controlled trials. *Frontiers in Pharmacology*, 13, 957483.
- Malik, T., Malik, A., & Abd-Elsayed, A. (2023). Pathophysiology of work-related neuropathies. *Biomedicines*, 11(6), 1745.
- Osiak, K., Elnazir, P., Walocha, J. A., & Pasternak, A. J. F. M. (2022). Carpal tunnel syndrome: state-of-the-art review. *Folia morphologica*, 81(4), 851-862.
- Sawangjit, R., Thongphui, S., Chaichompu, W., & Phumart, P. (2020). Efficacy and safety of mecobalamin on peripheral neuropathy: a systematic review and meta-analysis of randomized controlled trials. *The Journal of Alternative and Complementary Medicine*, 26(12), 1117-1129.
- Shelke, S., Ambade, R., & Shelke, A. (2023). From conservative measures to surgical interventions, treatment approaches for cubital tunnel syndrome: a comprehensive review. *Cureus*, 15(12).
- Sugiharto, H., Andini, D., & Puri, T. M. (2024). Perineural Injection of Mecobalamin Versus Dextrose 5% Against Clinical Changes and Electrophysiological Features of Carpal Tunnel Syndrome Patients at Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia. *Bioscientia Medicina: Journal of Biomedicine and Translational Research*, 8(6), 4485-4491.
- Talari, S. (2017). *Comparison of the Efficacy of Pregabalin, Methylcobalamin and Its Combination in the Treatment of Diabetic Peripheral Neuropathy in Type 2 Diabetes Mellitus Patients—A Prospective Study* (Doctoral dissertation, Rajiv Gandhi University of Health Sciences (India)).
- Wahab, K. W., Sanya, E. O., Adebayo, P. B., Babalola, M. O., & Ibraheem, H. G. (2017). Carpal tunnel syndrome and other entrapment neuropathies. *Oman medical journal*, 32(6), 449.
- Wainner, R. S., Fritz, J. M., Irrgang, J. J., Delitto, A., Allison, S., & Boninger, M. L. (2005). Development of a clinical prediction rule for the diagnosis of carpal tunnel syndrome. *Archives of Physical Medicine and Rehabilitation*, 86(4), 609-618.