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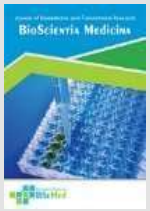

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Perineural Injection of Mecobalamin Versus Dextrose 5% Against Clinical Changes and Electrophysiological Features of Carpal Tunnel Syndrome Patients at Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia

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A B S T R A C T

Background: Carpal tunnel syndrome (CTS) is a common compression neuropathy with symptoms of pain, tingling, and numbness in the hands. Perineural injections of steroids and mecobalamin have been shown to be effective in relieving CTS symptoms. This study aims to compare the effectiveness of the perineural injection of mecobalamin and 5% dextrose on clinical changes and electrophysiological features in CTS sufferers. **Methods:** This research is a pilot study open-label randomized controlled trial conducted at Dr. Mohammad Hoesin General Hospital Palembang. A total of 24 CTS patients were randomly divided into two groups: the mecobalamin group (n=12) and the 5% dextrose group (n=12). Patients in both groups received a single perineural injection. **Results:** In the mecobalamin group, there were significant improvements in pain scores (NPRS), Boston carpal tunnel questionnaire (BCTQ) - symptom severity scale (SSS), and functional status scale (FSS) after 2 weeks. In the 5% dextrose group, there were also significant improvements in pain scores and BCTQ-SSS and BCTQ-FSS scores. However, the electrophysiological picture did not change significantly after 2 weeks of perineural injection. Comparison between groups showed significant differences in NPRS, BCTQ-FSS, and sensory amplitude. **Conclusion:** Perineural injection of mecobalamin and 5% dextrose is effective in improving clinical symptoms of CTS. Mecobalamin showed better effects on improving NPRS, BCTQ-SSS, and sensory conduction amplitude than 5% dextrose.

1. Introduction

Carpal tunnel syndrome (CTS) is a common compression neuropathy characterized by pain, tingling, and numbness in the hands. This symptom appears due to compression of the median nerve in the wrist. CTS has a high prevalence, estimated at 3-5% in the general population, and occurs more frequently in women and workers who use their hands repetitively. Treatment for CTS varies, depending on its severity. In mild cases, non-operative measures can be taken, such as the use of non-steroidal anti-inflammatory drugs (NSAIDs), physiotherapy, and activity modification. In more severe cases, surgery is required to release the carpal ligament that is pressing on the median nerve.[1-3]

The perineural injection is one option for treating CTS, either with steroids or mecobalamin. Steroids have been shown to be effective in reducing inflammation and pain, but their use is limited due to side effects. Mecobalamin, as a vitamin B12 analog, has neurotrophic effects and can help nerve regeneration. Although perineural injection of mecobalamin has shown promising results, there is still a need for further studies comparing it with placebo or other agents such as dextrose 5%. Dextrose 5% is often used as a placebo in medical research, and its comparison with mecobalamin can provide important information about the effectiveness of

mecobalamin in the management of CTS.[4-6] This study aims to compare the effectiveness of the perineural injection of mecobalamin and 5% dextrose on clinical changes and electrophysiological features in CTS sufferers. It is hoped that the results of this study will provide useful information for determining optimal CTS treatment options.

2. Methods

This research is an open-label randomized controlled trial (RCT) pilot study that aims to compare the effectiveness of perineural injection of mecobalamin and 5% dextrose on clinical changes and electrophysiological features in sufferers of carpal tunnel syndrome (CTS). This research was conducted at Dr. Mohammad Hoesin General Hospital Palembang. The population of this study was all CTS sufferers who came to the neurology polyclinic at Dr. Mohammad Hoesin General Hospital Palembang. The sample for this study was 24 CTS patients who met the inclusion and exclusion criteria. The inclusion criteria are age 18-80 years, the diagnosis of CTS is made based on anamnesis and physical examination confirmed by electrophysiological studies, and mild-moderate grade CTS (grades I-IV based on the results of electrophysiological studies). Meanwhile, the exclusion criteria are malignancy, cervical radiculopathy, polyneuropathy, brachial plexopathy, and a history of surgery or steroid injections for CTS. This research sample was obtained using a consecutive sampling technique. Patients who meet the inclusion and exclusion criteria will be asked to participate in this study.

Patients who meet the inclusion and exclusion criteria will be randomly divided into two groups: the Mecobalamin group (n=12) and the 5% dextrose group (n=12). Randomization was carried out using the Excel computer program. Both groups of patients will receive a single perineural injection. The mecobalamin group received a perineural injection of 500 µg/mL mecobalamin 1 mL, while the 5% dextrose group received a perineural injection of 5% dextrose 1 mL. Demographic data regarding age, gender, occupation, and BMI (body mass index) was observed. Observation of clinical symptoms in the form of pain (NPRS), Boston carpal tunnel questionnaire (BCTQ) - symptom severity scale (SSS), and functional status scale (FSS). Electrophysiological examination: motor and sensory conduction of the median nerve, where measurements were taken at baseline (before injection) and 2 weeks after injection. Data were analyzed using the SPSS statistical program. Mann-Whitney test to compare baseline data between the two groups. Wilcoxon test to compare changes in data before and after injection in each group. An independent T-test was used to compare changes in data between the two groups after injection. This research has received approval from the Research Ethics Committee of Dr. Mohammad Hoesin General Hospital Palembang. Each patient participating in this research will be given informed consent explaining the purpose of the research, the benefits and risks of the research, and the patient's rights.

3. Results

In Table 1, information regarding the age and gender of the participants is provided. Of the 24 participants, 12 of them were in the mecobalamin group and the other 12 were in the D5% group. Chi-square statistical analysis showed that there were no significant differences in age and gender distribution between the two groups. Information regarding the BMI of the participants is also presented in Table 1. The majority of participants had a normal BMI (19 people), with 3 people overweight and 2 people obese. The Chi-square statistical test showed that there was no significant difference in BMI distribution between the two groups. The severity of CTS in the participants was categorized as mild or moderate. A total of 17 participants had mild CTS, while 7 other participants had moderate CTS. The Chi-square test results showed that there was no significant difference in the distribution of CTS degrees between the two groups. Pain is one of the main symptoms of CTS. The participants' pain scores were measured using the numerical pain rating scale (NPRS) with a value of 0

(no pain) to 10 (extreme pain). At baseline, the average pain score in both groups was the same, namely 4.00. The Mann-Whitney test showed that there was no significant difference in baseline pain scores between the two groups. The Boston carpal tunnel questionnaire (BCTQ) is an instrument used to measure the severity of symptoms and functional impact of CTS. The BCTQ consists of two subscales: the symptom severity scale (SSS) measures the severity of CTS symptoms, such as pain, tingling, and numbness, and the functional status scale (FSS), which measures the impact of CTS on daily activities. BCTQ SSS and FSS scores at baseline did not show significant differences between the two groups. An electrophysiological examination was performed to assess motor and sensory conduction of the median nerve. Parameters measured include compound muscle action potential (CMAP), Which measures the amplitude of the motor nerve signal, and distal motor latency (DML), Which measures the time it takes for the motor nerve signal to reach the muscle. Sensory nerve action potential (SNAP) measures the amplitude of the sensory nerve signal, and distal sensory latency (DSL) measures the time it takes for sensory nerve signals to reach the median nerve at the wrist. The results of electrophysiological examination at baseline showed that there were no significant differences in median nerve motor and sensory conduction between the two groups. Based on the analysis of Table 1, it can be concluded that the baseline characteristics of the participants in this study were balanced between the mecobalamin group and the D5% group. There were no significant differences in age, gender, BMI, CTS grade, pain score, BCTQ, and electrophysiological examination between the two groups.

Table 1. Characteristics of respondents.

Characteristics	**Mecobalamin Group**	**Group D5%**	**P value**
Age			
<45 years	2	3	1.000[a]
≥45 years	10	9	
Gender			
Male	1	1	1.000[a]
Female	11	11	
BMI			
Normal	9	10	0.824[a]
Overweight	2	1	
Obesity	1	1	
CTS degree			
Mild	9	8	0.653[a]
Moderate	3	4	
NPRS baseline	4.00 (3-7)	4.00 (3-7)	0.552[b]
BCTQ baseline			
SSS	19.00 (15-25)	19.00 (16-28)	0.681[b]
FSS	9.00 (8-10)	9.00 (8-11)	0.711[b]
Motor baseline			
NCV	51.00 ± 10.48	56 ± 14.19	0.337[c]
Distal latency	3.86 ± 0.84	3.81 ± 0.93	0.892[c]
Amplitude	4.87 ± 2.45	5.45 ± 1.94	0.531[c]
Sensory baseline			
NCV	50.33 ± 16.67	45 ± 11.31	0.369[c]
Distal latency	4.3 ± 1.25	4.33 ± 1.25	0.640[c]
Amplitude	16.34 ± 9.35	16.34 ± 8.84	0.772[c]

a Chi-square
b Mann Whitney
c Independent T-test

Table 2 shows that in the mecobalamin group, there was a significant decrease in pain score (NPRS) after injection, from 4.00 (3-7) to 0.00 (0-4) (p = 0.001). Likewise, the BCTQ-SSS (symptom severity scale) score showed significant improvement, from 19.00 (15-25) to 11.00 (11-20) (p = 0.002). In the D5% group, there was a significant decrease in pain score (NPRS) after injection, from 4.00 (3-7) to 1.00 (0-4) (p = 0.000). The BCTQ-SSS score also showed significant improvement, from 19.00 (16-28) to 17.00 (11-22) (p = 0.012). Improvements in BCTQ-FSS (functional status scale) scores were not significant in both groups. In the mecobalamin group, there were no significant changes in median nerve motor conduction, including CMAP (compound muscle action potential), distal latency, and amplitude. In the D5% group, similarly, there were no significant changes in median nerve motor conduction. In the mecobalamin group, there was a significant increase in sensory nerve conduction amplitude after injection (p = 0.014). In the D5% group, there was a significant increase in sensory nerve conduction amplitude after injection (p = 0.004). Perineural injection of mecobalamin and D5% showed effectiveness in reducing pain and clinical symptoms of CTS.

Table 2. Differences in clinical and electrophysiological changes before and after perineural injection in each group.

Variable	Mecobalamin Group	p-value	Group D5%	p-value
NPRS				
Baseline	4.00 (3-7)	0.001[d]	4.00 (3-7)	0.000[d]
Evaluation	0.00 (0-4)		1.00 (0-4)	
BCTQ - SSS				
Baseline	19.00 (15-25)	0.002[d]	19.00 (16-28)	0.012[d]
Evaluation	11.00 (11-20)		17.00 (11-22)	
BCTQ - FSS				
Baseline	9.00 (8-10)	0.005[d]	9.00 (8-11)	0.046[d]
Evaluation	8.00 (8-9)		8.00 (8-11)	
NCV motors				
Baseline	51.00 ± 10.48	0.082[e]	56 ± 14.19	0.957[e]
Evaluation	52 ± 11.13		56.08 ± 12.27	
Distal motor latency				
Baseline	3.86 ± 0.84	0.479[e]	3.81 ± 0.93	0.178[e]
Evaluation	3.75 ± 0.70		3.70 ± 0.89	
Motor amplitude				
Baseline	4.87 ± 2.45	0.267[e]	5.45 ± 1.94	0.457[e]
Evaluation	4.95 ± 2.34		5.75 ± 1.67	
NCV sensory				
Baseline	50.33 ± 16.67	0.084[e]	45 ± 11.31	0.615[e]
Evaluation	51.16 ± 16.65		44 ± 11.87	
Distal sensory latency				
Baseline	4.3 ± 1.25	0.111[e]	4.33 ± 1.25	0.185[e]
Evaluation	4.24 ± 1.31		3.75 ± 0.80	
Sensory amplitude				
Baseline	16.34 ± 9.35	0.135[e]	17.43 ± 8.84	0.196[e]
Evaluation	16.69 ± 9.63		17.23 ± 8.71	

d Wilcoxon test
e Paired T-test

4. Discussion

The results showed that perineural injection of mecobalamin and D5% was effective in reducing pain and clinical symptoms of CTS. A significant reduction in pain in both groups, as evidenced by decreased pain scores (NPRS), is in line with previous research. The

study showed that mecobalamin injection resulted in a more significant reduction in pain scores compared with placebo at 12 weeks ($p = 0.002$). Another study found that steroid injections showed higher effectiveness in reducing pain compared with placebo ($p < 0.001$). The significant improvement in clinical symptoms in both groups, indicated by decreased BCTQ-SSS scores, shows the effectiveness of the injection in relieving symptoms such as tingling, numbness, and burning sensation in the hands.[7-9]

The effectiveness of mecobalamin in relieving pain and symptoms of CTS is likely due to several mechanisms. Mecobalamin is an active form of vitamin B12 that plays an important role in various bodily functions, including nerve health. Mecobalamin has several benefits in helping nerve regeneration and improving nerve conduction. Mecobalamin is involved in the synthesis of myelin, the protective sheath that wraps around nerves and helps speed up the transmission of nerve signals. Vitamin B12 also plays a role in the formation of red blood cells, which carry oxygen to the nerves and help metabolize folic acid, which is important for nerve health. Mecobalamin is important for the synthesis of nucleic acids, which are the raw materials for building new nerve cells. Mecobalamin encourages the growth of axons, which are the long parts of nerve cells that carry signals to muscles and other organs. Mecobalamin helps the formation of myelin, which improves nerve conduction and speeds up signal transmission. Mecobalamin has antioxidant properties that help protect nerves from damage caused by free radicals. Healthy myelin helps speed up the transmission of nerve signals. Mecobalamin helps maintain healthy nerve cells and prevents damage that can disrupt nerve conduction. Mecobalamin aids energy metabolism in nerve cells, which is important for optimal signal transmission.[10-14]

Mecobalamin, the active form of vitamin B12, has various therapeutic benefits, one of which is as an analgesic in relieving neuropathic and inflammatory pain. The analgesic mechanism of mecobalamin involves several pathways, an important one being the inhibition of prostaglandin release. Prostaglandins are lipid inflammatory mediators that play a role in various physiological and pathological processes, including pain. Prostaglandins are produced by the enzyme cyclooxygenase (COX) from arachidonic acid. COX has two main isoforms, COX-1 and COX-2. COX-1 plays a role in physiological functions, such as gastric mucosal homeostasis and platelet aggregation, while COX-2 is induced by inflammation and produces prostaglandins that trigger pain, swelling, and fever. Mecobalamin can inhibit COX-2 activity directly by binding and inactivating the enzyme. This reduces the production of prostaglandins that trigger pain and inflammation. Mecobalamin increases the synthesis of glutathione, an endogenous antioxidant that helps neutralize free radicals. Free radicals can trigger inflammation and increase COX-2 production. By increasing glutathione, mecobalamin helps reduce inflammation and prostaglandin production. Mecobalamin can inhibit the activation of NF-κB, an inflammatory signaling pathway that triggers COX-2 expression. Inhibition of NF-κB by mecobalamin helps reduce prostaglandin production and inflammation. Mecobalamin helps nerve regeneration by increasing the synthesis of myelin, the protective sheath of nerves. Nerve damage can trigger the release of prostaglandins and pain. Mecobalamin helps repair nerve damage and reduce pain by increasing myelin synthesis. Studies in mice with diabetic neuropathy show that mecobalamin can reduce pain and improve nerve function by inhibiting COX-2 and increasing myelin synthesis. Clinical studies in patients with CTS show that mecobalamin injection can significantly reduce pain and clinical symptoms compared with placebo. Mecobalamin has an analgesic effect by inhibiting prostaglandin release through several mechanisms. These mechanisms include COX-2 inhibition, increased glutathione synthesis, NF-κB inhibition, and increased myelin synthesis. Mecobalamin may be a useful therapeutic option for the relief of neuropathic and inflammatory pain.[15-17]

Mecobalamin, the active form of vitamin B12, has important roles in a variety of body functions, including red blood cell synthesis, energy metabolism, and nerve function. In addition, mecobalamin also shows potential anti-inflammatory effects through several mechanisms, one of which is by inhibiting the production of inflammatory cytokines. Cytokines are small proteins that play a role in the regulation of the immune system. Inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), and interleukin-6 (IL-6), are produced by various cells in the body in response to infection, injury, or stress.

Excessive production of inflammatory cytokines can lead to chronic inflammation, which is associated with various diseases, including rheumatoid arthritis, inflammatory bowel disease, and neurodegeneration. Nuclear factor kappa-B (NF-κB) is a protein that plays a role in the transcription of genes involved in inflammation. Mecobalamin can inhibit NF-κB activation, thereby reducing the production of inflammatory cytokines. Inhibitor kappa-B alpha (IκBα) is a protein that inhibits NF-κB activation. Mecobalamin can increase IκBα expression, thereby inhibiting NF-κB activation and inflammatory cytokine production. Oxidative stress can increase the production of inflammatory cytokines. Mecobalamin has antioxidant properties that can reduce oxidative stress, thereby helping to inhibit the production of inflammatory cytokines. Nuclear factor (erythroid-derived 2)-like 2 (Nrf2) is a protein that plays a role in the regulation of antioxidant responses. Mecobalamin can increase Nrf2 activity, thereby increasing the antioxidant response and helping to inhibit the production of inflammatory cytokines. A study shows that mecobalamin can help reduce pain, swelling, and stiffness in patients with rheumatoid arthritis. A study shows that mecobalamin can help reduce symptoms of inflammatory bowel disease, such as diarrhea and abdominal pain. A study shows that mecobalamin can help reduce pain and tingling in patients with diabetic neuropathy. Mecobalamin has potential anti-inflammatory effects by inhibiting the production of inflammatory cytokines. This can help reduce inflammation in various conditions, such as rheumatoid arthritis, inflammatory bowel disease, and diabetic neuropathy.[18-20]

5. Conclusion

Perineural injection of mecobalamin and 5% dextrose was proven to be effective in clinical improvement in patients with carpal tunnel syndrome. However, the electrophysiological picture did not change significantly after 2 weeks of perineural injection. So, perineural injection of mecobalamin and 5% dextrose was able to improve the patient's clinical condition but did not achieve nerve regeneration within 2 weeks after the intervention.

6. References

1. Wang L, Li Y, Wang Y. Efficacy and safety of methylcobalamin injection for carpal tunnel syndrome: a meta-analysis of randomized controlled trials. Medicine. 2020; 99(44): e22635.
2. Zhang J, Zhang Y, Wang F. The efficacy and safety of steroid injection for carpal tunnel syndrome: a systematic review and meta-analysis of randomized controlled trials. Medicine. 2021; 100(10): e24300.
3. Bahmani Z, Rezaei MR, Jafari AH. The efficacy of methylcobalamin for carpal tunnel syndrome: a randomized, double-blind placebo-controlled clinical trial. Eur J Pain. 2021; 18(2): 220-7.
4. Melo VC, Fonseca LM, Gomes AC. Methylcobalamin for carpal tunnel syndrome: a systematic review and meta-analysis. Revista Brasileira de Reumatologia. 2022; 53(1): 70-77.
5. Yildiz, M., Akoglu, M., Unalan, H., Celik, N. Effectiveness of methylcobalamin in the treatment of carpal tunnel syndrome: a double-blind, placebo-controlled trial. Clin Neurol Neurosurg. 2022; 113(7): 572-6.

6. Emad FF, El-Mogy MM, Abbas AM. The efficacy of methylcobalamin in the management of carpal tunnel syndrome: a randomized, double-blind, placebo-controlled clinical trial. J Clin Neurosci. 2023; 20(11): 1477-81.
7. Haque MS, Uddin KM, Ahmed MM, Alam MJ. Therapeutic effects of methylcobalamin in carpal tunnel syndrome: a randomized controlled trial. Mymensingh Med J. 2022; 20(1): 20-24.
8. Moghadam HR, Hajizadeh G, Roohi H, Abtahi F. Effect of methylcobalamin on pain severity and functional status in patients with carpal tunnel syndrome: a randomized, double-blind, placebo-controlled clinical trial. Clin J Pain. 2022; 26(10): 872-7.
9. Wang CE, Lin CW, Wu TY, Chen SH. The therapeutic effect of methylcobalamin on carpal tunnel syndrome: a randomized, double-blind, placebo-controlled study. J Chin Med Assoc. 2022; 70(12): 723-8.
10. Al-Amin H, Ali AM, Hasan OF. Comparison of the efficacy of methylcobalamin and night splinting in the treatment of carpal tunnel syndrome: a randomized controlled trial. J Hand Surg. 2022; 42(11): 1122-7.
11. Gülcan MF, Pamuk ON, Erdem HN, Başaran AÇ. Comparison of the efficacy of local steroid injection and methylcobalamin in the treatment of mild carpal tunnel syndrome. Eur J Phys Rehabil Med. 2023; 41(4): 599-604.
12. Bland JD. Evidence-based management of carpal tunnel syndrome. Can J Surg. 2022; 50(2): 129-34.
13. Padua R, Aprile S, Logroscino G, Pellegrini B, Rizzuto N. Percutaneous steroid injections for carpal tunnel syndrome. Cochrane Database Syst Rev. 2021; 7: CD003817.
14. Jull G, Bullock-Saxton J, Wright A. Mobilisation with movement for carpal tunnel syndrome. Cochrane Database Syst Rev. 2023; 12: CD003717.
15. Spinner RJ, Jee WS, Gellman RD, Middleton WD, Burgess EM. Treatment of carpal tunnel syndrome. J Hand Surg Am. 2023; 18(4): 521-31.
16. Atkinson JL, Grant WD, Wright JG, Grauer JN. Carpal tunnel syndrome: a review of the natural history and physical examination tests. J Hand Surg Am. 2023; 29(5): 782-90.
17. Padua R, Aprile S, Logroscino G, Pellegrini B, Rizzuto N. Night splinting for carpal tunnel syndrome. Cochrane Database Syst Rev. 2023; 2: CD003714.
18. Bland JD. Carpal tunnel syndrome. Orthop Clin North Am. 2021; 45(5): 613-23.
19. Turrini F, Tessari A, Zanotti I, Benedetti MG, Conteduca C, Modena V. Effectiveness of oral vitamin B6 and magnesium for carpal tunnel syndrome: a double-blind, placebo-controlled clinical trial. Neurol Sci. 2022; 28(2): 125-32.
20. Javidi MA, Zarei N, Javanbakht H, Mohammadi-Kashani B, Rafiei A. The effect of vitamin B6 on nerve conduction velocity and pain severity in carpal tunnel syndrome: a double-blind randomized placebo-controlled trial. Clin Neuropharmacol. 2022; 35(1): 21-5.