The Importance of Alpha-Lipoic Acid and Vitamin B Complex in Treating Carpal Tunnel Syndrome in a Patient Diagnosed with Diabetes Mellitus – A Case Report

Uloga alfa-lipoične kiseline i vitamina skupine B u liječenju karpalnog sindroma u bolesnika s dijabetesom – prikaz bolesnika

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SUMMARY Carpal tunnel syndrome represents a set of symptoms and signs caused by the compression of the distal portion of the median nerve in the carpal tunnel. It is important in everyday clinical practice since it is the most frequent mononeuropathy that significantly influences the functionality and the quality of daily activities. The conventional treatment of carpal tunnel syndrome consists of (based on severity and duration of symptoms) different therapies, such as: corticosteroids, immobilization or surgery. This is a case report of a 54-year-old patient, suffering from diabetes mellitus for many years. After clinical and electromyographic confirmation of moderate chronic carpal tunnel syndrome, and because of the existing polyneuropathy, the patient has been treated with alpha-lipoic acid and vitamin B complex in recommended therapeutic doses for several months. An improvement has been verified clinically and electromyographically. The result indicates the possibility of successful therapeutic application of alpha-lipoic acid and vitamin B complex in diabetic patients with mild to moderate carpal tunnel syndrome. Further randomized controlled clinical studies are needed to confirm this.

KEY WORDS: carpal tunnel syndrome, diabetes mellitus, alpha-lipoic acid, vitamin B complex

SAŽETAK Karpalni sindrom čini skupina simptoma uzrokovanih kompresijom distalnog dijela nervusa medianusa u karpalnom tunelu. Sindrom je važan u svakodnevnoj kliničkoj praksi jer se radi o učestaloj mononeuropatiji koja znatno utječe na funkcionalnost i kvalitetu svakodnevnih aktivnosti. Konvencionalno liječenje karpalnog sindroma ovisi o jačini i trajanju simptoma i uključuje raznoliku terapiju: kortikosteroide, imobilizaciju i operaciju. U radu prikazujemo bolesnika u dobi od 54 godine s dugogodišnjim dijabetesom. Nakon kliničke i elektromiografske dijagnoze srednje teškoga kroničnog karpalnog sindroma i zbog prisutne neuropatije bolesnik je liječen alfa-lipoičnom kiselinom i vitaminima skupine B u preporučenim dozama tijekom nekoliko mjeseci. Poboljšanje je potvrđeno i klinički i elektromiografski. Rezultati upućuju na mogućnost uspješne aplikacije alfa-lipoične kiseline i vitamina skupine B u bolesnika s dijabetesom i blagim do srednje teškim karpalnim sindromom. Potrebna su daljnja kontrolirana randomizirana klinička istraživanja koja će to potvrditi.

KLJUČNE RIJEČI: karpalni sindrom, dijabetes, alfa-lipoična kiselina, vitamini skupine B

Introduction

Carpal tunnel syndrome represents a set of symptoms and signs caused by the compression of the distal portion of the median nerve in the carpal tunnel, defined in 1951 by Brian McArdle (1, 2).

Epidemiologic data indicate that carpal tunnel syndrome is the most frequent mononeuropathy, prevalent in 2.7% of general population. Women are three times more likely than men to develop carpal tunnel syndrome and it mostly occurs in the 5th and 6th decade of life (3). Carpal tunnel syndrome has a significant negative effect on the functionality and the quality of daily activities (4).

There is a large number of potential causes of carpal tunnel syndrome (Table 1.) (1, 3) which affect the nerve and/or its environment by raising intracanalicular pressure above 30 mm/Hg (normal values being 7 – 8 mm/Hg) and create a disproportion between nerve volume and the tunnel space. Myelin remodeling, damage of axonal transport,

TABLE 1. Causes of carpal tunnel syndrome

CAUSES	
Idiopathic	
Congenital	anomalies of muscles, tendons, bones and ligaments on the level of the tunnel
Metabolic	thyroid dysfunction, hyperparathyroidism, acromegaly, pregnancy, contraceptives use, menopause, diabetes mellitus, hemodialysis, obesity
Tumors	
Inflammatory	rheumatoid arthritis, gouty arthritis, myositis, scleroderma, amyloidosis, systemic lupus erythematosus, sarcoidosis
Traumatic	cumulative trauma, fractures, hematoma, burns, immobilizations
Degenerative	
Infective	abscess, Lyme disease, tuberculosis, histoplasmosis, septic arthritis
Vascular	
Neuropathic	thrombosis, aneurysm of the persistent median artery

the initiation of the cascade of ischemic nerve changes and the creation of intraneural connective tissue are the consequence (5, 6). Diabetes mellitus causes carpal tunnel syndrome (and other disorders, such as polyneuropathy) more frequently than other potential causes (7 – 9). After eliminating the causal factor, a remyelinization of the nerve is possible after several weeks (5).

The main symptoms include paresthesia and pain in hands, in the area of innervation of the median nerve (except for the area of thenar), with a possible propagation towards the shoulder, intensifying during the night and when performing certain activities (holding a telephone or a book). Furthermore, the weakness of thenar is possible, accompanied by positive pathognomonic test results (Phalen's maneuver, Tinel's sign, carpal-compression test, as well as rarely used reverse Phalen's maneuver, hand elevation test, tourniquet test, Okutsu test) (1, 10, 11). Sensory symptoms are missing in the case of pure motor carpal tunnel syndrome (3).

Possible differential-diagnostic conditions include neuropathy of the median nerve of other locations (entrapment on the level of Struthers' ligament, pronator syndrome, syndrome of the anterior interosseous nerve), damage of brachial plexus, radiculopathy (primarily of C6 and C7), initial forms of certain polyneuropathies (multifocal motor polyneuropathy, multifocal acquired demyelinating sensorimotor polyneuropathy), as well as migraines, focal epileptic seizures and, transient ischemic attacks (1, 5).

Diagnosis of carpal tunnel syndrome is primarily based on clinical symptoms, with electromyoneurographic examination representing the diagnostic method of choice. In addition to the confirmation of the diagnosis it delivers information on the degree of severity (mild, moderate or severe), the duration (frequently subacute or chronic), and other accompanying conditions. After the examination, it is necessary to perform X–ray examination of the carpal area and routine laboratory tests (3, 12). Ultrasonic examination of peripheral nerves has become a complementary method to electromyographic examination, helping not only to verify the diagnosis, but also to observe the structure of the median nerve and its environment, as well as to determine the degree of severity (mild, moderate or severe) (13, 14).

Conventional treatment can be non-operative and operative. For treatment of mild and moderate carpal, tunnel syndrome and in the absence of a direct external compression, conservative therapy, consisting of immobilization and a perineural application of corticosteroids presents the first choice. Immobilization is performed by wearing a special-purpose orthosis for the wrist during sleep for the period of three weeks. The application of corticosteroid therapy is contraindicated in the case of disturbance in skin integrity in the area of the carpal tunnel in the presence of local infections, and in - case of injuries of the median nerve, ligaments or blood vessels. Surgical treatment is performed in cases where a conservative treatment has been tried unsuccessfully for the period of six months, where there is a direct external cause of compression and in the case of a severe carpal tunnel syndrome. It can be performed through an open or an endoscopic approach (3, 10, 15).

Treatment success rates vary, from 40% with conservative therapy to 85% with surgical treatment (16).

Alpha-lipoic acid and vitamin B complex (especially pyridoxine and thiamine) are proven concepts in the treatment of diabetic polyneuropathy (7, 17). Alpha-lipoic acid acts by multiple mechanisms (antioxidant effect and neurotrophic induction). Pyridoxine influences the metabolism of lipids and myelinisation, whereas thiamine exhibits antioxidant effect, without any significant contraindications or side effects (7, 17). We used the same concept with our patient to achieve treatment effect on mild and moderate carpal tunnel syndrome originating from diabetes (4, 18).

TABLE 2. Laboratory findings

Name	Value	Name	Value
SE	14 mm/h	Cholesterol	7.63 mmol/L
Erythrocytes	4.69 x10^9/L	Triglycerides	1.78 mmol/L
Hemoglobin	143 g/L	Glucose	8.69 mmol/L
Hematocrit	43.9%	CK	65 U/L
MCV	93.6 f.L	LDH	120 U/L
Leukocytes	5.65x10^9/L	Urea	5.3 mmol/L
Thrombocytes	256x10^9/L	Creatinine	64 µmol/L
ALT	39 U/L	CRP	1.4 mg/L
AST	12 U/L	Fibrinogen	2.96 g/L
GGT	35 U/L	Na	143 mmol/L
Total bilirubin	5.7 µmol/L	Cl	107 mmol/L
Direct bilirubin	1.9 µmol/L	K	4.74 mmol/L
Uric acid	268 µmol/L	Ca	2.46 mmol/L
TSH	2.8 mU/L	P	1.07 mmol/L
iPTH	74.40 pg/ml	RF	<0.5
Total proteins	73.2 g/L	Urine	
Albumin	54.1 %	Negative for bilirubin	ph 5.5
$Alpha_1$	4.1 %	Clear, yellow color	Negative for proteins
$Alpha_2$	7.8 %	Glucose 8.69++++ > = 55 mmol/L	Proteins 24 hours 0.27 g/dU
Beta	17.4 %	Negative for ketones	Specific weight 1025
Gamma	12.12 %	Creatinine 24 hours 15.0 mmol/dU	Negative for urobilinogen

Case Report

A 54 year old, male patient with occupational history of working as a waiter and who prequalified 10 years ago to work with milling machines and driving a tractor. The patient is dominantly right handed.

Six and half years prior to the presentation in our clinic, the patient experienced "sensory changes" that started in his toes. Six months before the first examination the patient started experiencing consistent numbness and pain in one hand (in the innervated region of N. medianus), weakness ("when cutting cabbage") with no worsening of symptoms during the night. Patient also mentions history of neck and low back pain.

The patient has been suffering from diabetes mellitus for 25 years and has been treated with antidiabetic medications (metformin 500 mg; glimepiride 3 mg). No specific habits.

He has high lipid levels and high blood pressure. He broke his left arm above the carpal area in his twenties.

Patient denies similar carpal tunnel syndrome related difficulties in the family. Family history of diabetes mellitus.

Neurological results show regular bulbomotorics and symmetric innervation of the mimical musculature on the level of cranial nerves. Indolence of neck in anteflexion, without meningeal stimulus. No pain in the roots of the spinal nerves while stretching. Pronation test of the upper limbs shows the right arm in semipronation. Symmetric myotatic reflexes. Negative

TABLE 3. Electromyoneurographic examination

Nerve conduction studies I			Nerve conduction studies II			
Nerve	Distal latency (msec)	Conduction velocity (m/sec)	Nerve	Distal latency (msec)	Conduction velocity (m/sec)	
Median left side	5.36	47.0	Median left side	4.80	49.68	Motor study
Ulnar left side	3.64	41.0	Ulnar left side	2.86	47.11	
Tibial right side	5.10	36.0	Tibial right side	5.96	32.41	
Tibial left side	5.18	35.0	Tibial left side	5.92	36.97	
Nerve conduction studies I			Nerve conduction studies II			
Median left side	7.16	18.2	Median left side	4.68	29.91	Sensory study
Ulnar left side	2.38	42.0	Ulnar left side	2.00	55.00	
Tibial right side	6.48	32.40	Tibial right side	6.48	32.41	
Tibial left side	5.18	36.00	Tibial left side	5.68	36.97	
Median left side	33.85		Median left side	30.31		F – wave latency
Ulnar left side	37.80		Ulnar left side	29.96		
Tibial right side	60.80		Tibial right side	66		
Tibial left side	61.55		Tibial left side	69		

Electromyographic needle examination I						
Muscle	Insercional activity	Spontaneus activity	Recruitment	Duration	Amplitude	Polyphasia
Right abductor pollicis brevis	Normal	0	Normal	Long	+2	Normal
Right abductor digiti minimi	Normal	0	Normal	Long	+2	Normal
Right pronator teres	Normal	0	Normal	Long	+2	Normal
Right abductor hallucis brevis	Normal	0	Normal	Long	+1	Normal
Left abductor hallucis brevis	Normal	0	Normal	Long	+2	Normal
Electromyographic needle examination II						
Muscle	Insercional activity	Spontaneus activity	Recruitment	Duration	Amplitude	Polyphasia
Right abductor pollicis brevis	Normal	0	Normal	Long	+2	Normal
Right abductor digiti minimi	Normal	0	Normal	Long	+2	Normal
Right pronator teres	Normal	0	Normal	Long	+1	Normal
Right abductor hallucis brevis	Normal	0	Normal	Long	+1	Normal
Left abductor hallucis brevis	Normal	0	Normal	Long	+1	Normal

Bikele's sign. Positive Tinel's sign on the right side. Furthermore, equilaterally positive Phalen's maneuver. Normal results of the Mingazzini test in the lower limbs. Preserved rough muscular force. Lower patellar tendon reflex on the left side. Plantar response of skin in the type of flexor. Cerebral tests without problems. On the level of sensibility – hypesthesia of the hand in the region of innervation of the median nerve, as well as irregular surface sensibility in the "stocking-glove" pattern, with present trophic changes. Preserved speech and swallowing, as well as control of sphincters.

No qualitative – quantitative changes in the psychological status. In the somatic status, the patient is afebrile, asthenic, euhydrated, cardiopulmonary compensated. Blood pressure is 100/80 mm/Hg. Based on the anamnestic data, clinical examination and specifically noticed pathognomonic signs, we suspect carpal tunnel syndrome, which is why electromyographic examination was performed according to the suggested procedure for evaluating carpal tunnel syndrome (Table 3.).

As the electromyographic parameters indicated the presence of moderate chronic carpal tunnel syndrome and moderate chronic radiculopathy C6, which lead to the conclusion of the existence of moderate double crush syndrome in the area of sensorimotor polyneuropathy, specific additional diagnostic procedures were initiated, with the aim of determining the etiologic basis.

The values obtained using routine laboratory tests are presented in Table 2.

During the ultrasonography of peripheral nerves the cross sectional area of both median nerves on the level of the carpal tunnel was around 10 mm^2. Both nerves were normally mobile during flexor tendon movements. No tumor changes, pathologic liquid collections or other pathologic changes were noticed in the carpal regions.

Radiography of the carpal region of both hands did not show any significant pathologic changes. Other than a discreetly uneven contour of the right stiloid extension no other pathologic changes could be noticed on the carpal bones.

Radiography of cervical spine on the level from the fifth to seventh cervical vertebra shows spondylotic changes with significantly narrowed intervertebral space. No other significant pathological changes were noticed on other levels. Based on clinical examination and conducted tests, the diagnosis of a moderate chronic carpal tunnel syndrome of diabetic origin and moderate chronic radiculopathy C6 (probably oxriginating from compression and degeneration, as well as double crush syndrome in the area of sensorimotor polyneuropathy caused by diabetes) was set. A peroral therapy of alpha-lipoic acid in therapeutic morning dose of 600 mg, as well as a dose of vitamin B complex in the morning and at noon was introduced.

After three months of monitoring, a significant subjective improvement was noticed in the form of reduced numbness and pain as well as increased grip strength. Furthermore, an improvement in terms of a lack of pathognomonic signs (Tinel's sign, Phalen's maneuver) has been registered on the basis of objective findings, but some other changes found during the first examination have been verified (pronation test of the upper limbs shows the right arm in semipronation; lower patellar tendon reflex on the left side, hypesthesia of the hand in the region of innervation of the median nerve, as well as irregular surface sensibility in the "stocking-glove" pattern, with present trophic changes).

Comparison of electromyographic findings at first and control visit show improvements in terms of carpal tunnel syndrome, whereas the other aspects of electromyoneurographic examination remain unaltered (Table 3.).

Discussion

Diabetes mellitus is one of most frequent causes of the most common mononeuropathy the carpal tunnel syndrome.

The strongest evidence for the clinical use of alpha-lipoic acid and vitamin B complex is derived from double blind, placebo controlled trials showing significant improvement in polyneuropathies associated with diabetes (19, 20).

The primary effect is achieved by raising the internal resistance of the nerve trough different mechanism such as regeneration trough endogenous antioxidants such as vitamins C and E, neutralization of free radicals, regulation of gene transcription and inhibition of nuclear factor kappa B activation involved in processes of synaptic plasticity and memory.

Although rare, there are clinical studies that prove efficacy of application of alpha-lipoic acid with vitamin B complex, gamma-linoleic acid and curcumin phytosome in patients with carpal tunnel syndrome. Different combinations were used, but not those with only alpha-lipoic acid and vitamin B complex (4, 21).

The abovementioned information provides an explanation for the positive effect in treating mild to moderate carpal tunnel syndrome of diabetic origin.

Conclusion

Alpha-lipoic acid given daily at dose of 600 mg, together with recommended dose of vitamin B complex for three months for the treatment of moderate chronic carpal tunnel syndrome of diabetic origin, led to an improvement of clinical signs and symptoms and was confirmed by electromyographic examination.

The addition of alpha-lipoic acid and vitamin B complex represents a valuable addition to conventional therapy of carpal tunnel syndrome caused by diabetes mellitus.

Based on our experience in treating carpal tunnel syndrome of diabetic origin with alpha-lipoic acid and vitamin B complex, we believe that randomized controlled clinical studies would also prove the positive effect.

REFERENCES

1. Preston CD, Shapiro EB. Electromyography and Neuromuscular Disorders. USA: Butterworth-Heinemann; 1998.
2. Victor M, Ropper AH. Adams and Victor's Principles of neurology. USA: McGraw-Hill; 2001.
3. Dumitri D, Amato AA, Zwarts JM. Electrodiagnostic Medicine, 2nd edition. USA: Hanley and Belfus, Inc.; 2002.
4. Di Geronimo G, Fonzone Caccese A, Caruso L, Soldati A, Passaretti U. Treatment of carpal tunnel syndrome with alpha-lipoic acid. European Review for Medical and Pharmacological Sciences 2009;13:133–139.
5. Apostolski S. Mehanizam nastanka i opšte karakteristike tunel sindroma. Centar za kontinuiranu edukaciju u zdravstvu Medicinskog fakulteta Univerziteta u Novom Sadu; 2010.
6. Gorsché R. Carpal Tunnel Syndrome. The Canadian Journal of CME; 2001.
7. Cvijanović M. Diabetesna neuropatija. Novi Sad: Medicinski fakultet Novi Sad; 2010.
8. Burner WT, Rosenthal KA. Diabetes and Rheumatic Diseases. Current Opinion in Rheumatology 2009;21(1):50–54.
9. Damjan I, Cvijanović M, Erak M. Značaj elektromiografskog pregleda u dijagnostikovanju i praćenju hronične inflamatorne demijelinizacione polineuropatije. Med pregl 2010;63(7–8):559–564.
10. Bland JDP. Carpal-tunnel.net. Available from: URL: https://www.carpal-tunnel.net/; 2011.
11. Yoshida A, Okutsu I, Hamanaka I. A New Diagnostic Provocation Test for Carpal Tunnel Syndrome: Okutsu Test. Hand Surg.; 2010.
12. Rigler I, Podnar S. Kratek presejalni vprašalnik za paciente s sindromom zapestnega prehoda. Zdrav Vestn 2009;78:73–8.
13. Peer S, Bodner G. High-Resolution Sonography of the Peripheral Nervous System, 2nd Revised Edition. Berlin Heidelberg: Springer-Verlag; 2008.
14. Karadağ YS, Karadağ O, Çiçekli E, Oztürk S, Kiraz S, Ozbakir S, Filippucci E, Grassi W. Severity of Carpal tunnel syndrome assessed with high frequency ultrasonography. Rheumatol Int 2010;30(6):761–5.
15. Jovanović M. Hirurško lečenje tunel sindroma. Centar za kontinuiranu edukaciju u zdravstvu Medicinskog fakulteta Univerziteta u Novom Sadu; 2010.
16. Podnar S. Predlog priporočil za obravnavo bolnikov s sindromom zapestnega prehoda v Sloveniji. Zdrav Vestn 2008;77:103–9.
17. Singleton JR, Smith AG. The Diabetic Neuropathies: Practical and Rational Therapy. Seminars in Neurology 2012;32:196–203.
18. Ryan-Harshman M, Aldoori W. Carpal tunnel syndrome and vitamin B6. Canadian Family Physician 2007;53:1161–1162.
19. Ziegler D, Nowak H, Kempler P, Vargha P, Low PA. Treatment of symptomatic diabetic polyneuropathy with the antioxidant alpha-lipoic acid: a meta-analysis. Diabet Med 2004;21(2):114–21.
20. Mijnhout GS, Kollen BJ, Alkhalaf A, Kleefstra N, Bilo HJG. Alpha-Lipoic Acid for Symptomatic Peripheral Neuropathy in Patients with Diabetes: A Meta-Analysis of Randomized Controlled Trials. Int J Endocrinol 2012:456279.
21. Pajardi G, Bortot P, Ponti V, Novelli C. Clinical usefulness of oral supplementation with alpha-lipoic Acid, curcumin phytosome, and B-group vitamins in patients with carpal tunnel syndrome undergoing surgical treatment. Evid Based Complement Alternat Med 2014;2014:891310. doi: 10.1155/2014/891310.

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